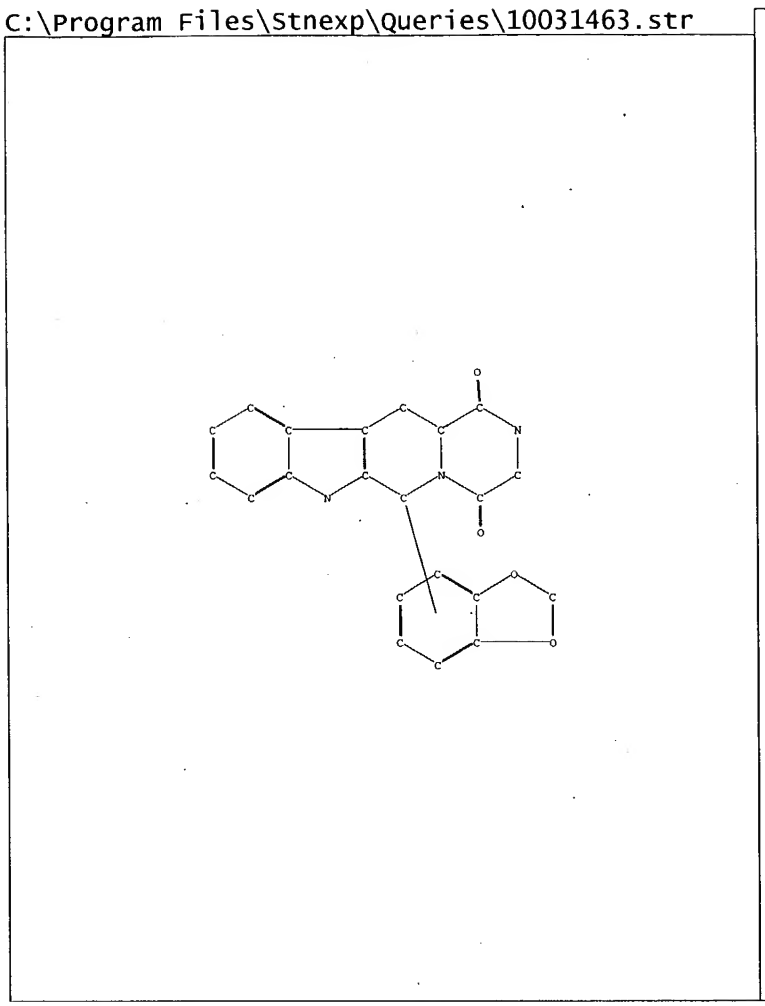
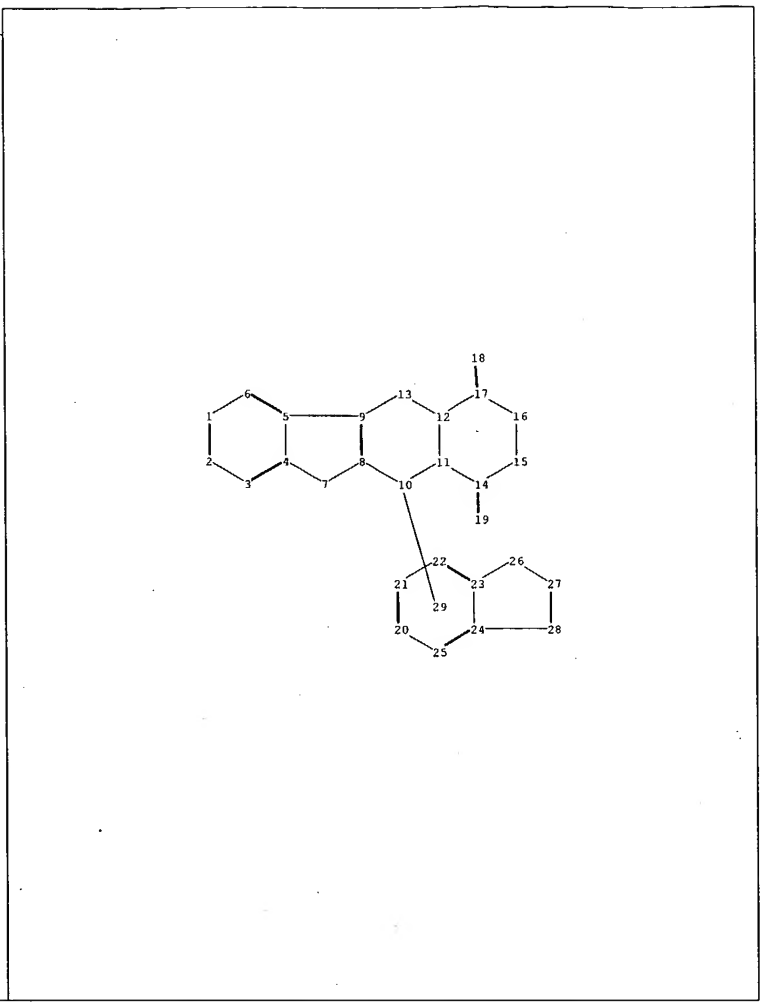
C:\Program Files\Stnexp\Queries\10031463.str





chain nodes :
18 19
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 20 21 22 23 24 25 26 27
28
chain bonds :
14-19 17-18
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9 8-10 9-13 10-11 11-12 11-14 12-13
12-17 14-15 15-16 16-17 20-21 20-25 21-22 22-23 23-24 23-26 24-25 24-28 26-27
27-28
exact/norm bonds :
4-7 7-8 8-9 8-10 9-13 10-11 11-12 11-14 12-13 12-17 14-15 14-19 15-16 16-17
17-18 23-26 24-28 26-27 27-28
exact bonds :
5-9
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 20-21 20-25 21-22 22-23 23-24 24-25
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS 20:Atom
21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:CLASS

10/031463

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=> s l1
SAMPLE SEARCH INITIATED 15:57:43 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     16 TO ITERATE

100.0% PROCESSED      16 ITERATIONS                                  7 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           80 TO      560
PROJECTED ANSWERS:               7 TO      298

L3            7 SEA SSS SAM L1

=> d l3 1-7
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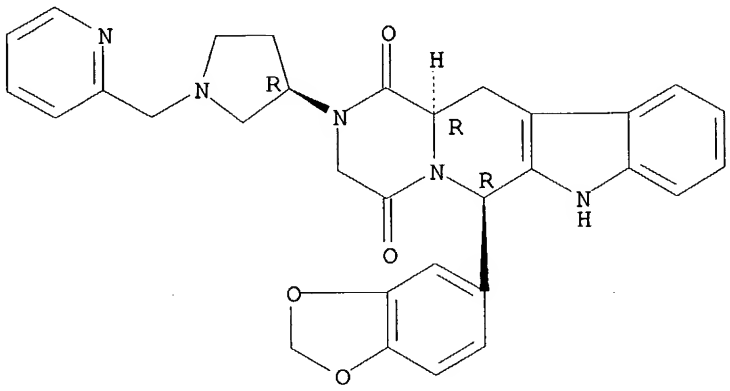
L3 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2003 ACS on STN
RN 574730-08-8 REGISTRY
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(3R)-1-(2-pyridinylmethyl)-3-pyrrolidinyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H29 N5 O4
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

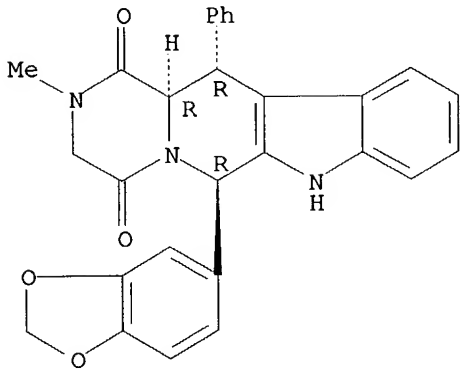


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2003 ACS on STN
RN 477978-88-4 REGISTRY
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-12-phenyl-, (6R,12R,12aR)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H23 N3 O4
SR CA
LC STN Files: CA, CAPLUS

Relative stereochemistry.

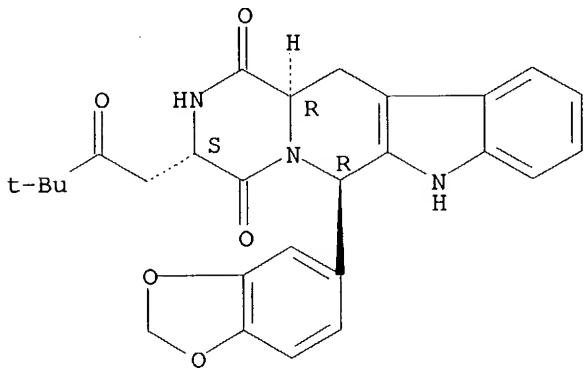


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2003 ACS on STN
RN 395665-80-2 REGISTRY
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-3-(3,3-dimethyl-2-oxobutyl)-2,3,6,7,12,12a-hexahydro-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H27 N3 O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

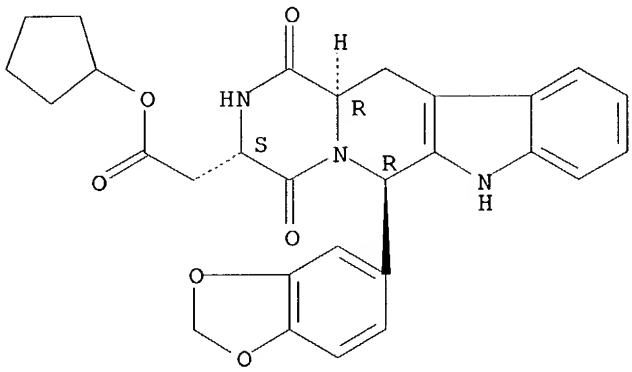


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2003 ACS on STN
RN 395665-78-8 REGISTRY
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, cyclopentyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H27 N3 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

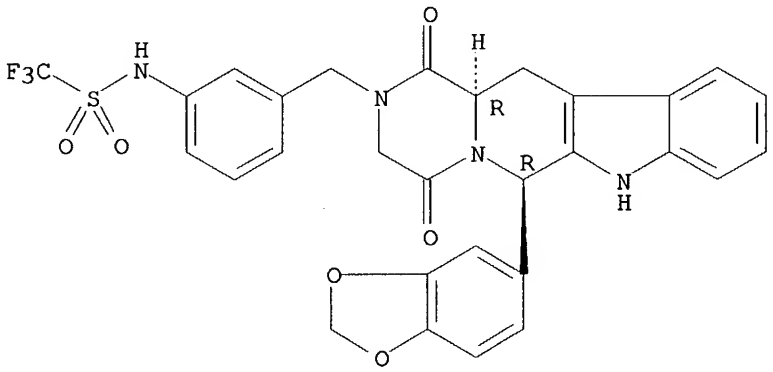


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2003 ACS on STN
RN 385770-93-4 REGISTRY
CN Methanesulfonamide, N-[3-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]phenyl]-1,1,1-trifluoro- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C29 H23 F3 N4 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

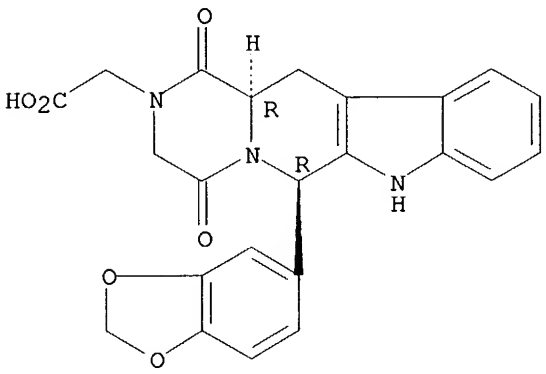


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2003 ACS on STN
RN 385770-82-1 REGISTRY
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H19 N3 O6
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

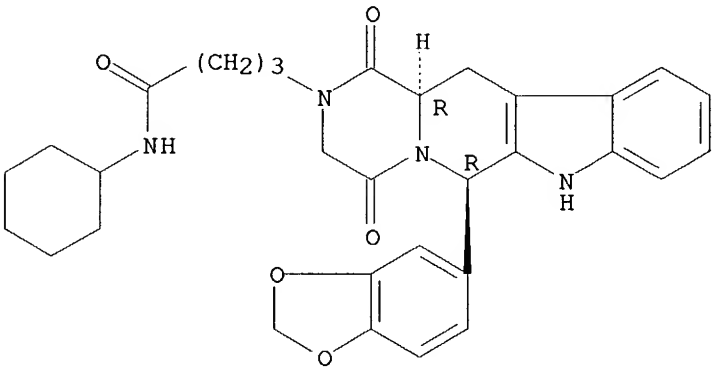


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2003 ACS on STN
RN 385770-34-3 REGISTRY
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-butanamide, 6-(1,3-benzodioxol-5-yl)-N-cyclohexyl-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H34 N4 O5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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FULL SEARCH INITIATED 15:58:33 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    379 TO ITERATE

100.0% PROCESSED     379 ITERATIONS                          207 ANSWERS
SEARCH TIME: 00.00.01

L4          207 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                160.71     160.92

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FILE LAST UPDATED: 30 Dec 2003  (20031230/ED)

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  substance identification.


=> s l4
L5          79 L4
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=> d l5 1-79 bib abs hit str
'STR' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
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PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
              SCAN must be entered on the same line as the DISPLAY,
              e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, IPC, and NCL

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
              containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
              its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
              its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

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codes.  For a list of the display field codes, enter HELP DFIELDS at
an arrow prompt (=>).  Examples of formats include: TI; TI,AU; BIB,ST;
TI,IND; TI,SO.  You may specify the format fields in any order and the
information will be displayed in the same order as the format
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FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC
to view a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):end

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L5 ANSWER 1 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:950772 CAPLUS
DN 140:747
TI Phosphodiesterase 5 inhibitor-ACE inhibitor combination for the treatment of hypertension
IN Fox, David Nathan Abraham; Hughes, Bernadette
PA Pfizer Limited, UK; Pfizer Inc.
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003099194	A2	20031204	WO 2003-IB1889	20030509

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

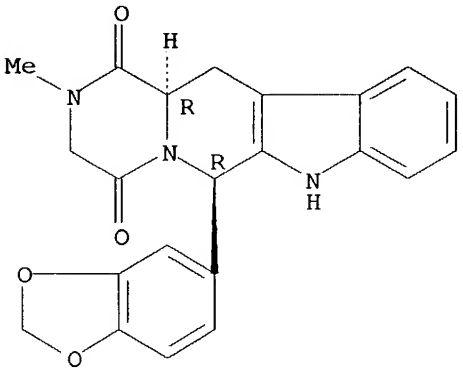
PRAI GB 2002-11919 A 20020523
GB 2002-29784 A 20021220

AB The invention discloses combinations comprising (a) an inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5 (PDE5) inhibitor and (b) an inhibitor of angiotensin converting enzyme (ACE) for treating hypertension.

IT **171596-29-5**, Tadalafil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 5 inhibitor-ACE inhibitor combination for treatment of hypertension)

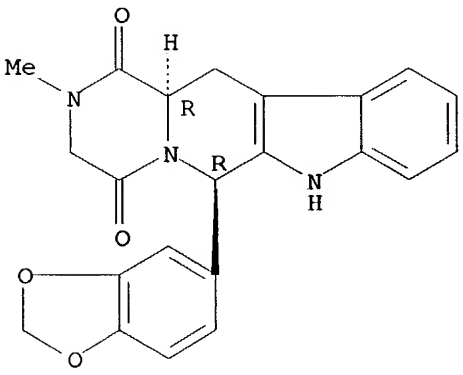
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 2 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:914111 CAPLUS
DN 139:374117
TI Tadalafil
AU Curran, Monique P.; Keating, Gillian M.
CS Adis International Limited, Auckland, N. Z.
SO Drugs (2003), 63(20), 2203-2212
CODEN: DRUGAY; ISSN: 0012-6667
PB Adis International Ltd.
DT Journal; General Review
LA English
AB A review. Tadalafil is a selective phosphodiesterase type 5 inhibitor that is effective in men with mild-to-severe erectile dysfunction (ED), including those with diabetes mellitus. The improvement in the erectile function domain score on the International Index of Erectile Function (IIEF) and the percentage of sexual intercourse attempts marked by successful vaginal penetration and completion was significantly greater with on-demand (not more than once daily) tadalafil 10 or 20mg than placebo in trials of 12 wk' duration. Improvement in scores on other domains of the IIEF and the percentage of pos. responses to a Global Assessment Question measuring erection improvement were also significantly greater with on-demand tadalafil than placebo. The adverse events assocd. with tadalafil were generally mild to moderate and decreased in frequency with continued administration. The most commonly reported adverse events were headache and dyspepsia. The incidence of cardiovascular adverse events was not significantly different in tadalafil or placebo recipients.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase type 5 inhibitor tadalafil in men with erectile dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



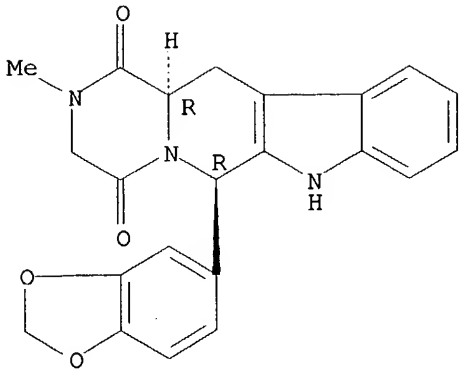
L5 ANSWER 3 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:818141 CAPLUS
DN 139:312448
TI Methods of treating medication-, substance-, disease-, and other medical condition-related sexual dysfunction
IN Shapira, Nathan Andrew
PA University of Florida, USA
SO U.S. Pat. Appl. Publ., 12 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003195186	A1	20031016	US 2003-411644	20030410
WO 2003086372	A2	20031023	WO 2003-US10994	20030410

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-371666P P 20020410
AB Many males and females experience sexual dysfunction either caused or made worse by medications, other substances, diseases, and other medical conditions. Currently, there is need for addnl. treatment alternatives for these patients' sexual dysfunction. The subject invention provides a novel treatment for these individuals with sexual dysfunction by inhibiting the enzyme that breaks down acetylcholine (a compd. that helps modulate normal sexual function) and elevates acetylcholine levels in the body. The acetylcholinesterase inhibitor is selected from the group consisting of donepezil, galantamine, tacrine, eptastigmine, physostigmine, rivastigmine, metrifonate, neostigmine, huperzine A, and combinations thereof.
IT **171596-29-5**, Tadalafil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acetylcholinesterase inhibitor in combination with other actives for treatment of sexual dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).


O
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L5 ANSWER 4 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:796498 CAPLUS
DN 139:286351
TI Use of methylene blue and related compounds to prevent or reverse an exaggerated hemodynamic reaction
IN Juneau, Martin; Tanguay, Jean-Francois; Brouillette, Denis
PA Institut de Cardiologie de Montreal/Montreal Heart Institute, Can.
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

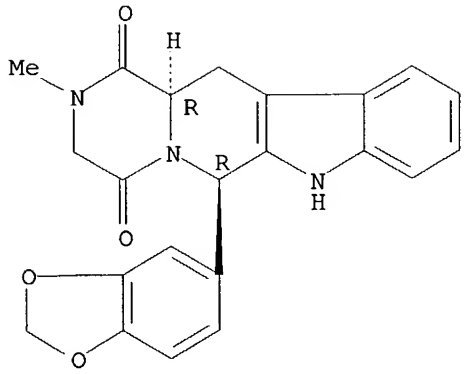
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003082296	A1	20031009	WO 2003-CA456	20030328
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003219495	A1	20031127	US 2003-401819	20030328
PRAI CA 2002-2379211	A	20020328		

AB The present invention relates to the use of the dye methylene blue (MB) or a related compd. to prevent or reverse an exaggerated hemodynamic reaction in animals in need thereof, including humans. More specifically, the present invention concerns the use of MB or a related compd. to prevent or reverse hypotension, unstable angina, myocardial infarction or shock caused by the concomitant ingestion of a phosphodiesterase inhibitor, such as sildenafil citrate, and a NO-donor, such as L-arginine, or an org. nitrate, such as nitroglycerin. MB reversed drops in blood pressure caused by the combined administration of sildenafil citrate and nitroglycerin in pigs and dogs.

IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(phosphodiesterase inhibitor, prevention or reversal of hemodynamic problems caused by; methylene blue and related compds. for prevention or reversal of exaggerated hemodynamics)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

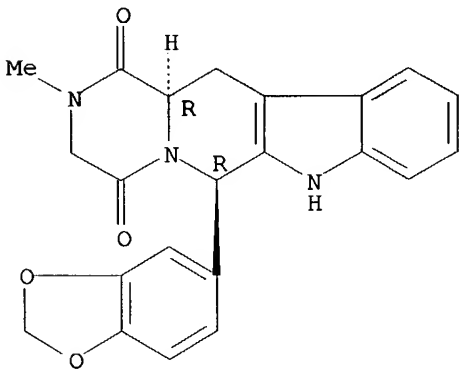
Absolute stereochemistry. Rotation (+).



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:784105 CAPLUS
TI The discovery of tadalafil: a novel and highly selective PDE5 inhibitor. 2: 2,3,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione analogue
AU Daugan, Alain; Grondin, Pascal; Ruault, Cecile; Le Monnier de Gouville, Anne-Charlotte; Coste, Herve; Linget, Jean Michel; Kirilovsky, Jorge; Hyafil, Francois; Labaudiniere, Richard
CS Centre de Recherches, Laboratoire GlaxoSmithKline, Les Ulis, 91951, Fr.
SO Journal of Medicinal Chemistry (2003), 46(21), 4533-4542
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Modification of the hydantoin ring in the previously described lead compd. 2a has led to the discovery of compd. 12a, tadalafil, a highly potent and highly selective PDE5 inhibitor. The replacement of the hydantoin in compd. 2a by a piperazinedione ring led to compd. cis-11a which showed similar PDE5 inhibitory potency. Introduction of a 3,4-methylenedioxy substitution on the Ph ring in position 6 led to a potent PDE5 inhibitor cis-11c with increased cellular potency. Optimization of the chain on the piperazinedione ring led to the identification of the racemic cis-N-Me deriv. 11i. High diastereospecificity for PDE5 inhibition was obsd. in the piperazinedione series with the cis-(6R,12aR) enantiomer displaying the highest PDE5 inhibitory activity. The piperazinedione 12a, tadalafil (GF196960), has been identified as a highly potent PDE5 inhibitor (IC50 = 5 nM) with high selectivity for PDE5 vs. PDE1-4 and PDE6. Compd. 12a displays 85-fold greater selectivity vs. PDE6 than sildenafil 1. 12a showed profound and long-lasting blood pressure lowering activity (30 mmHg/>7 h) in the spontaneously hypertensive rat model after oral administration (5 mg/kg).
IT **171596-29-5P**, Tadalafil
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(discovery of PDE5 inhibitor tadalafil and analogs)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

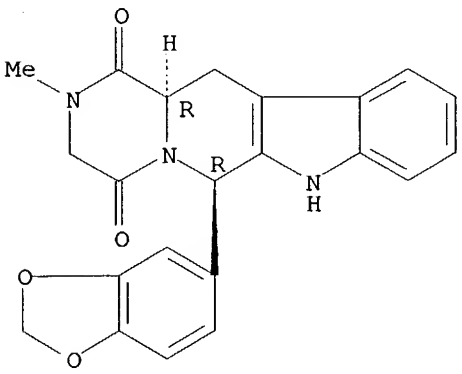


IT **171488-03-2P 171488-17-8P 171596-27-3P**

171596-28-4P 629652-62-6P 629652-67-1P
629652-68-2P 629652-71-7P 629652-72-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(discovery of PDE5 inhibitor tadalafil and analogs)

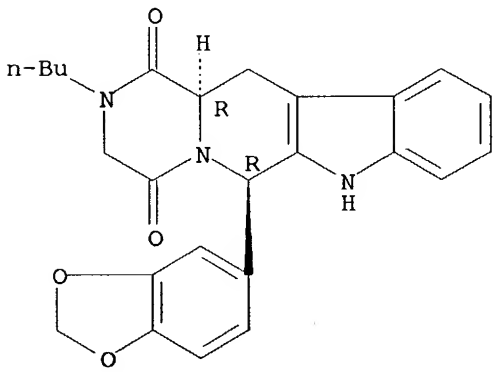
RN 171488-03-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



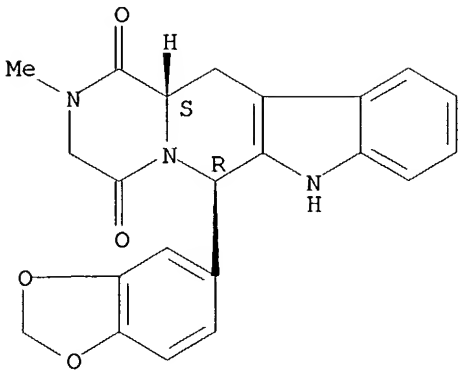
RN 171488-17-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



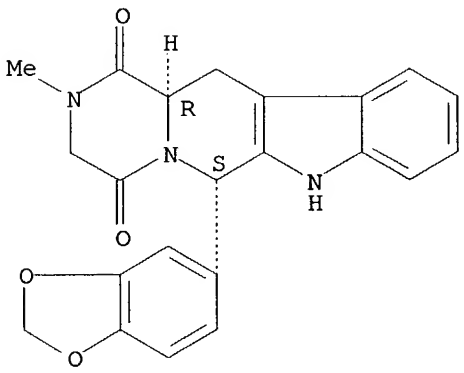
RN 171596-27-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



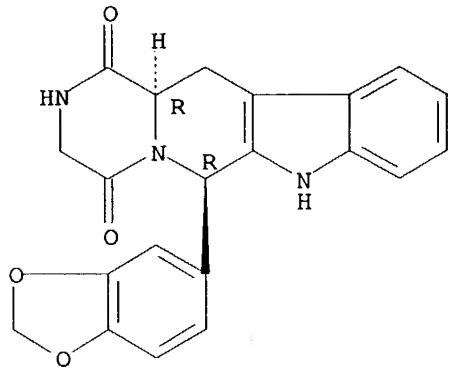
RN 171596-28-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6S,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 629652-62-6 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

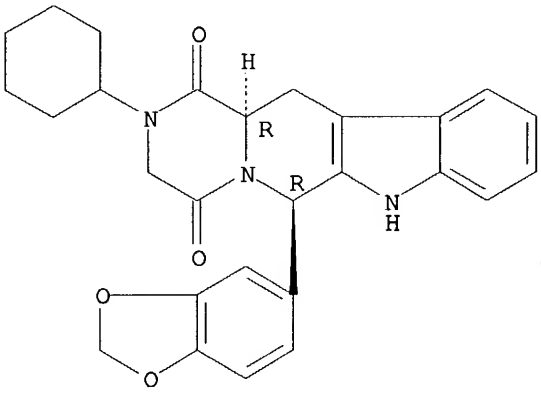
Relative stereochemistry.



RN 629652-67-1 CAPLUS

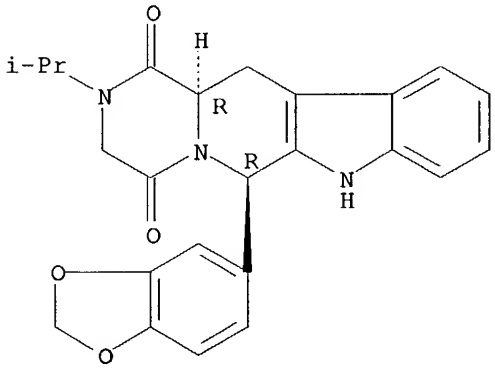
CN INDEX NAME NOT YET ASSIGNED

Relative stereochemistry.



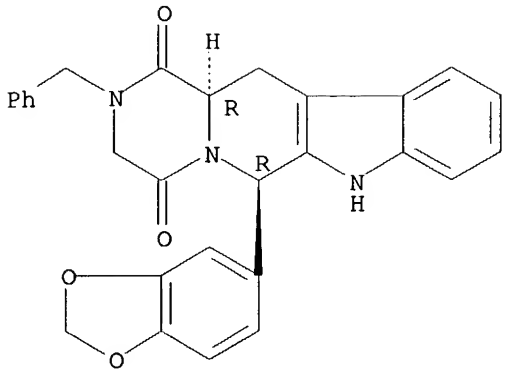
RN 629652-68-2 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Relative stereochemistry.



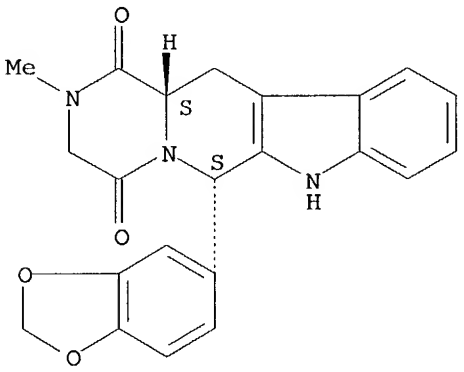
RN 629652-71-7 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Relative stereochemistry.



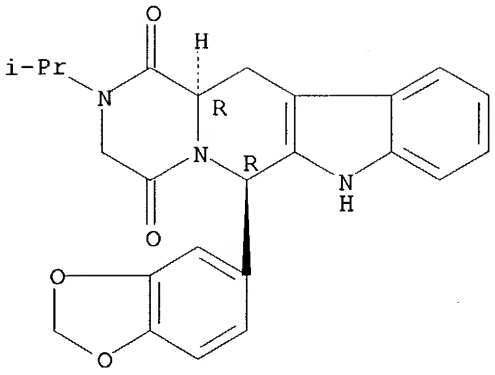
RN 629652-72-8 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



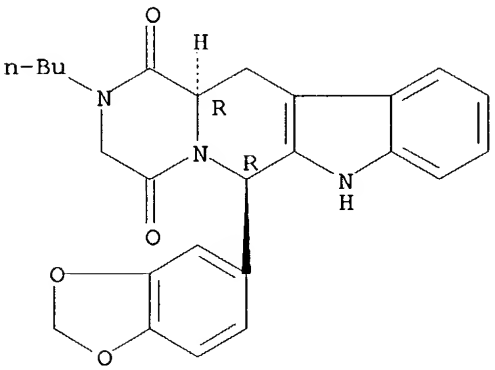
IT **171596-30-8 171596-31-9 171596-36-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discovery of PDE5 inhibitor tadalafil and analogs)
RN 171596-30-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(1-methylethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



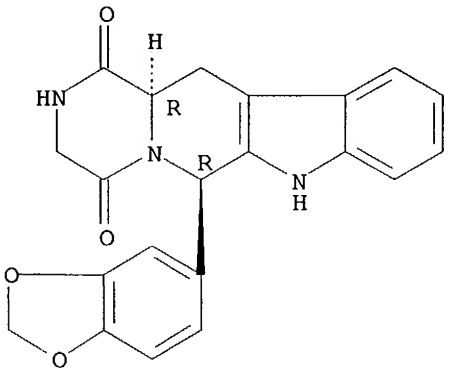
RN 171596-31-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



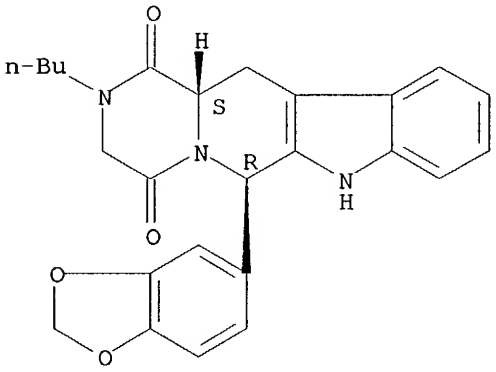
RN 171596-36-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **171488-16-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(discovery of PDE5 inhibitor tadalafil and analogs)
RN 171488-16-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

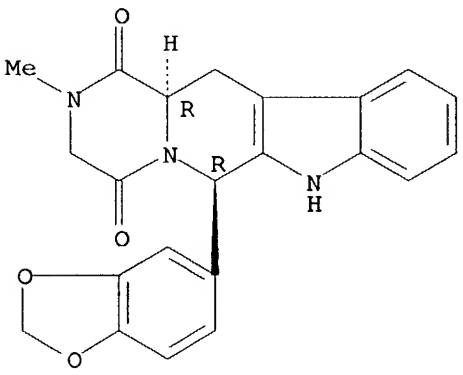
Relative stereochemistry.



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:784091 CAPLUS
TI The discovery of tadalafil: a novel and highly selective PDE5 inhibitor. 1: 5,6,11,11a-tetrahydro-1H-imidazo[1',5':1,6]pyrido[3,4-b]indole-1,3(2H)-dione analogues
AU Daugan, Alain; Grondin, Pascal; Ruault, Cecile; Le Monnier de Gouville, Anne-Charlotte; Coste, Herve; Kirilovsky, Jorge; Hyafil, Francois; Labaudiniere, Richard
CS Centre de Recherches, Laboratoire GlaxoSmithKline, Les Ulis, 91951, Fr.
SO Journal of Medicinal Chemistry (2003), 46(21), 4525-4532
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Starting from Et .beta.-carboline-3-carboxylate (.beta.-CCE), 1, a modest inhibitor of type 5 phosphodiesterase (PDE5), a series of functionalized tetrahydro-.beta.-carboline derivs. has been identified as a novel chem. class of potent and selective PDE5 inhibitors. Optimization of the side chain on the hydantoin ring of initial lead compd. 2 and of the arom. ring on position 5 led to the identification of compd. 6e, a highly potent and selective PDE5 inhibitor, with greater selectivity for PDE5 vs. PDE1-4 than sildenafil. Compd. 6e demonstrated a long lasting and significant blood pressure lowering effect after iv administration in the spontaneously hypertensive rat model but showed only moderate oral in vivo efficacy.
IT **171596-29-5**, Tadalafil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis and structure activity relationship of tadalafil indoledione analogs as PDE5 inhibitor)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

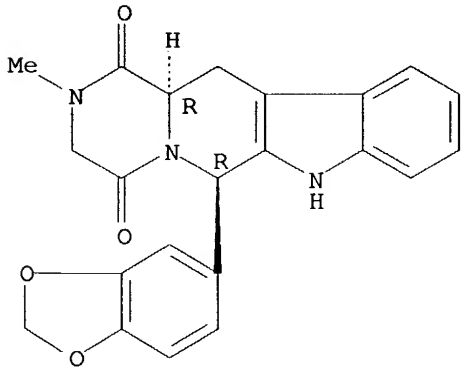
Absolute stereochemistry. Rotation (+).



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:692406 CAPLUS
DN 139:303761
TI Structure of the catalytic domain of human phosphodiesterase 5 with bound drug molecules
AU Sung, Byung-Je; Hwang, Kwang Yeon; Jeon, Young Ho; Lee, Jae Il; Heo, Yong-Seok; Kim, Jin Hwan; Moon, Jinho; Yoon, Jung Min; Hyun, Young-Lan; Kim, Eunmi; Eum, Sung Jin; Park, Sam-Yong; Lee, Jie-Oh; Lee, Tae Gyu; Ro, Seonggu; Cho, Joong Myung
CS The Division of Drug Discovery, CrystalGenomics Inc., Jeonmin-dong, Yuseong-gu, Daejeon, 305-390, S. Korea
SO Nature (London, United Kingdom) (2003), 425(6953), 98-102
CODEN: NATUAS; ISSN: 0028-0836
PB Nature Publishing Group
DT Journal
LA English
AB Phosphodiesterases (PDEs) are a superfamily of enzymes that degrade the intracellular second messengers cAMP and cGMP. As essential regulators of cyclic nucleotide signaling with diverse physiol. functions, PDEs are drug targets for the treatment of various diseases, including heart failure, depression, asthma, inflammation and erectile dysfunction. Of the 12 PDE gene families, cGMP-specific PDE5 carries out the principal cGMP-hydrolyzing activity in human corpus cavernosum tissue. It is well known as the target of sildenafil citrate (Viagra) and other similar drugs for the treatment of erectile dysfunction. Despite the pressing need to develop selective PDE inhibitors as therapeutic drugs, only the cAMP-specific PDE4 structures are currently available. Here we present the three-dimensional structures of the catalytic domain (residues 537-860) of human PDE5 complexed with the three drug mols. sildenafil, tadalafil (Cialis) and vardenafil (Levitra). These structures will provide opportunities to design potent and selective PDE inhibitors with improved pharmacol. profiles.
IT **171596-29-5P**, Cialis
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structure of catalytic domain of human phosphodiesterase 5 with bound drug mols.)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

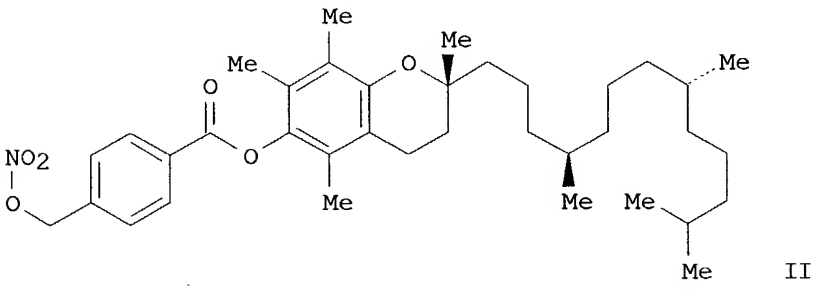


RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:652131 CAPLUS
DN 139:214237
TI Preparation of nitrate prodrugs able to release nitric oxide in a controlled and selective way and their use for prevention and treatment of inflammatory, ischemic and proliferative diseases
IN Scaramuzzino, Giovanni
PA Italy
SO Eur. Pat. Appl., 313 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1336602	A1	20030820	EP 2002-425075	20020213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI EP 2002-425075		20020213		

GI



II

AB New pharmaceutical compds. of general formula F-(X)q (I) [q = 1-5, preferably 1; F is chosen among drugs such as .delta.-tocopherol, clidanac, diethylhomospermine, glucosamine, thymocartin, vofopitant, etc.; X is chosen among 4 groups M, T, V, and Y where M = ONO2, nitrate salt, nitrite ester, ONO, thoinitrite, SNO, etc., T = OR1-M, OR1OR1-M, SR1NR2R1-M, NR2R1-M, NR2R1SR1-M, etc., R1 = satd. or unsatd., linear or branched alkylene, having 1 to 21 carbon atoms or a satd. or unsatd., optionally heterosubstituted or branched cycloalkylene, having 3 to 7 carbon atoms or an optionally heterosubstituted arylene having 3 to 7 carbon atoms; R2 = H, satd. or unsatd., linear or branched 1-21 carbon atom alkyl, satd. or unsatd. optionally heterosubstituted or branched 3-7 carbon cycloalkyl, optionally heterosubstituted 3-7 carbon aryl; R1, R2 = OH, SH, F, Cl, Br, OPO3H2, CO2H, etc.; bond between F and T = carboxylic ester, carboxylic amide, glycoside, azo, thioester, sulfonic ester, etc.; V = Z-M2, OZ-M2, NR2Z-M2, R1Z-M2, OR1-M2, OR1Z-M2, M2 = M, R1-M, OR1-M, SR1-M, NR2R1-M; ZM2 = COCH2CH(M2)CH2N+Me3, COCH2CH2COM2, COCH(NHR2)CH2M2, etc.; Y = 4-COC6H4CH2ONO2, O(CH2)4ONO2, COCH(NH2)CH2ONO2, 3-OC6H4CH2ONO2, etc.] were prepd. For example, .alpha.-tocopherol reacted with 4-HO2CC6H4CH2ONO2 to give the nitroxymethyl deriv. II. The compds. of general formula I are nitrate prodrugs which can release nitric oxide in vivo in a controlled and selective way and without hypotensive side effects and for this reason they are useful for the prepn. of medicines for prevention and treatment of inflammatory, ischemic, degenerative and

proliferative diseases of musculoskeletal, tegumental, respiratory, gastrointestinal, genito-urinary and central nervous systems.

IT **586349-81-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

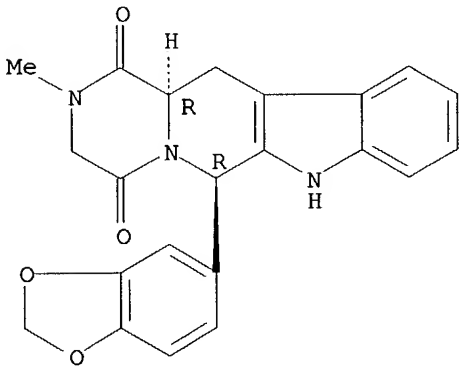
RN 586349-81-7 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)-, mononitrate (9CI) (CA INDEX NAME)

CM 1

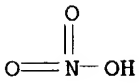
CRN 171596-29-5
CMF C22 H19 N3 O4

Absolute stereochemistry. Rotation (+).



CM 2

CRN 7697-37-2
CMF H N O3



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:590998 CAPLUS
DN 139:128037
TI Use of acetylcholine esterase antagonists to treat insulin resistance
IN Lautt, Wayne W.
PA Diamedica Inc., Can.
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

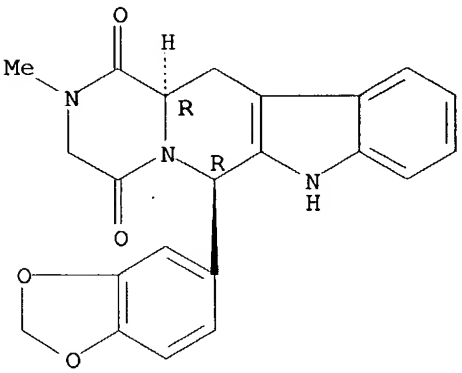
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003061648	A1	20030731	WO 2003-CA78	20030127
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003235609	A1	20031225	US 2003-350478	20030124
PRAI	US 2002-350958P	P	20020125		

AB A method is provided for reducing insulin resistance in a mammalian subject, comprising administering a suitable acetylcholine esterase antagonist.

IT **171596-29-5**, , Tadalafil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acetylcholine esterase antagonists for treatment of insulin resistance, and use with other agents)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:590992 CAPLUS
DN 139:128035
TI Use of phosphodiesterase antagonists to treat insulin resistance
IN Lautt, Wayne W.; Macedo, Paula
PA Diamedica Inc., Can.
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003061638	A2	20030731	WO 2003-CA77	20030127
	WO 2003061638	A3	20031002		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

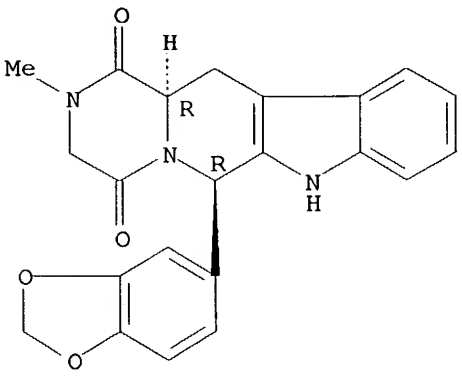
	US 2003181461	A1	20030925	US 2003-350070	20030124
PRAI	US 2002-350954P	P	20020125		

AB There is provided the use of a phosphodiesterase antagonist to reduce insulin resistance, and to amplify the effect of nitric oxide on skeletal muscle insulin-mediated glucose uptake in a mammal. In some instances, the antagonist is targeted to the liver. In some instances, the insulin resistance is hepatic insulin sensitizing substance ('HISS') dependant insulin resistance.

IT **171596-29-5**, Tadalafil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of phosphodiesterase antagonists to treat insulin resistance)

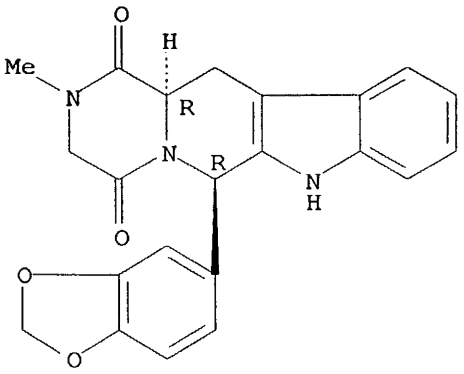
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 11 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:496779 CAPLUS
DN 139:316393
TI Novel treatment options for overlapping yet distinct erectile dysfunction and andropause syndromes
AU Tan, Robert S.
CS Geriatrics & Men's Health Programs, Department of Family & Community Medicine, University of Texas Medical School, Houston, TX, 77030, USA
SO Current Opinion in Investigational Drugs (Thomson Current Drugs) (2003), 4(4), 435-438
CODEN: COIDAZ; ISSN: 1472-4472
PB Thomson Current Drugs
DT Journal; General Review
LA English
AB A review. The Food & Drug Administration has recently approved, or is in the process of approving newer drugs such as the phosphodiesterase inhibitors and apomorphine to treat men's health issues including erectile dysfunction. Increasing age results in a gradual hypogonadal state in men, for which different novel delivery systems of androgens are currently offered for the symptomatic patient. As such, many men are presenting to healthcare practitioners for the first time. The age of presentation for erectile dysfunction and andropause often overlaps, typically in the fifties and beyond, therefore, it makes sense to screen for erectile dysfunction in andropause patients and vice versa. Erectile dysfunction is usually a harbinger for other illnesses, such as coronary heart disease and depression. The hypogonadal state, likewise, could be a harbinger for other ill health states in men, including obesity, depression, osteoporosis and possibly memory loss. While the newer treatments for erectile dysfunction and andropause are distinctly different and targeted at symptom relief, the presentation of the patient with erectile dysfunction or andropause offers an excellent opportunity for screening for other health states and health education strategies.
IT **171596-29-5**, Cialis
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel treatment options for overlapping yet distinct erectile dysfunction and andropause syndromes)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:491029 CAPLUS
DN 139:63337
TI Use of selective phosphodiesterase 5 (PDE5) inhibitors in the treatment of pulmonary diseases having a ventilation-perfusion mismatch
IN Ghofrani, Ardeschir; Grimminger, Friedrich Josef; Schudt, Christian
PA Altana Pharma AG, Germany
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

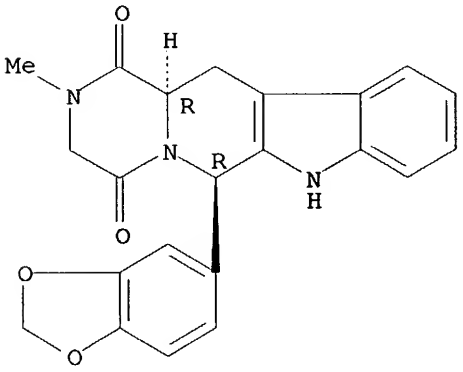
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003051346	A2	20030626	WO 2002-EP14279	20021214

W: AE, AL, AU, BA, BR, CA, CN, CO, CU, DZ, EC, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, TN, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR

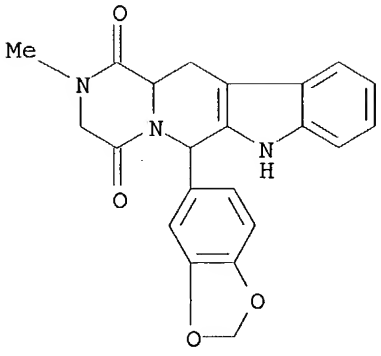
PRAI EP 2001-129951 A 20011217
EP 2002-9555 A 20020426
EP 2002-23936 A 20021025

AB The invention discloses the use of PDE5 inhibitors for the treatment of patients having a pulmonary disorder in which in which a pulmonary ventilation-pulmonary perfusion mismatch is present.
IT **171596-29-5**, Tadalafil **304683-09-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 5 inhibitors for treatment of pulmonary disease with ventilation-perfusion mismatch)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 304683-09-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl- (9CI) (CA INDEX NAME)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L5 ANSWER 13 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:450774 CAPLUS
DN 139:17600
TI Kit for reducing aching caused by phosphodiesterase V (PDE5) inhibitors
IN Abel, Samantha; Ellis, Peter
PA Pfizer Limited, UK; Pfizer Inc.
SO Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

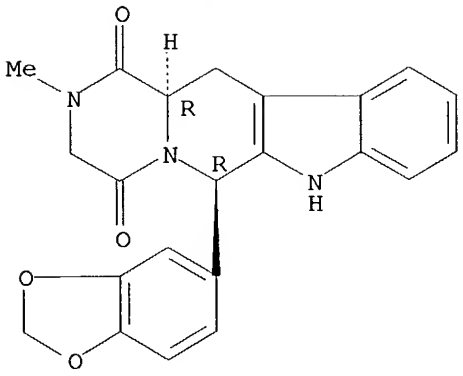
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1317924	A1	20030611	EP 2002-258123	20021126
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	WO 2003047588	A1	20030612	WO 2002-IB4933	20021122
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	JP 2003192614	A2	20030709	JP 2002-349628	20021202
	US 2003124150	A1	20030703	US 2002-310608	20021205
PRAI	GB 2001-29274	A	20011206		
	US 2002-355286P	P	20020208		

AB The invention relates to kits, and aspects thereof, for reducing or eliminating the aching assocd. with the administration of multiple doses of a PDE5 inhibitor, the kits comprising a plurality of pharmaceutical compns. for sequential administration over a period of time which compns. comprise increasing amts. of PDE5 inhibitor starting with an amt. which gives a suboptimal response and ending with an amt. which gives an optimal response.

IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(kit for reducing aching caused by phosphodiesterase V inhibitors)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

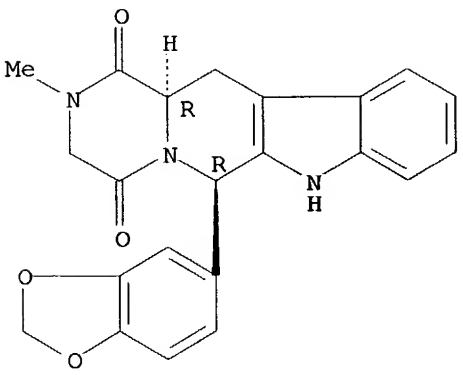
Absolute stereochemistry. Rotation (+).



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:419328 CAPLUS
DN 139:357661
TI The etiology of erectile dysfunction and mechanisms by which drugs improve erection
AU Galle, Gunter; Trummer, Harald
CS Department of Urology, Karl-Franzens University of Graz, Austria
SO Drugs of Today (2003), 39(3), 193-201
CODEN: MDACAP; ISSN: 0025-7656
PB Prous Science
DT Journal; General Review
LA English
AB A review. Following the National Institutes of Health (NIH) consensus conference in 1988, erectile dysfunction is defined as the consistent inability to maintain a penile erection sufficient for adequate sexual relations. The advances in basic and clin. research during the last two decades have led to the development of several new treatment options for erectile dysfunction, including new pharmacol. agents for intracavernosal, intraurethral and oral use. The recent advent of medical therapy and the poor results of long-term follow-up in reconstructive vascular surgery, have significantly modified the medical management of this disorder. Discussion of erectile dysfunction has increased, information about erectile dysfunction is increasingly available, training in erectile dysfunction was improved and last, but not least, the no. of patients seeking help for erectile dysfunction is growing, because satisfactory sexual function is an important part of a couple's healthy relationship and ongoing quality of life.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drugs- anr other factors-induced erectile dysfunction and mechanisms by which drugs improve erection)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

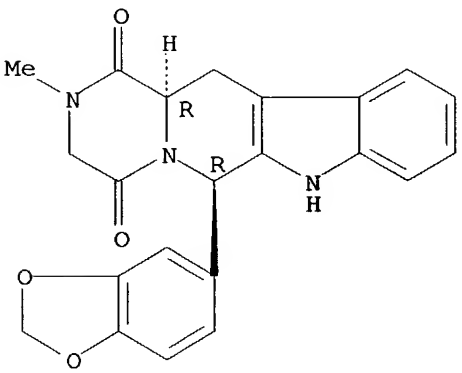
Absolute stereochemistry. Rotation (+).



RE.CNT 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:409897 CAPLUS
DN 139:127241
TI Tadalafil, a further innovation in the treatment of sexual dysfunction
AU Pomerol, Jose Maria; Rabasseda, Xavier
CS Fundacio Puigvert, Barcelona, Spain
SO Drugs of Today (2003), 39(2), 103-113
CODEN: MDACAP; ISSN: 0025-7656
PB Prous Science
DT Journal; General Review
LA English
AB A review. In recognition of the large no. of sufferers of sexual dysfunction worldwide, and the variety of etiologies of the condition, investigation into effective pharmacol. agents has been expanded. One method of intervention is inhibition of phosphodiesterase type 5 (PDE5), an action which has already been exploited with a considerable degree -- though not complete -- of success. A no. of new agents that inhibit PDE5 are under development. Notable among these is tadalafil, which has demonstrated a high level of selectivity for PDE5 over the other phosphodiesterases and has shown efficacy in improving erectile function and sexual satisfaction in phase III trials. Throughout the clin. development program for tadalafil, the drug has been well tolerated and without serious side effects. The manufacturer, Lilly ICOS, received a letter of approval from the US Food and Drug Administration on Apr. 30, 2002, for use of the drug as a treatment for erectile dysfunction. Lilly ICOS hopes to market tadalafil, with the trade name Cialis, in the USA in 2003.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tadalafil for treatment of sexual dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:396889 CAPLUS
DN 138:401744
TI Preparation of polycyclic guanine derivative phosphodiesterase V inhibitors
IN Asberom, Theodros; Clader, John W.; Hu, Yueqing; Pissarnitski, Dmitri A.; Stamford, Andrew W.; Xu, Ruo
PA Schering Corporation, USA
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

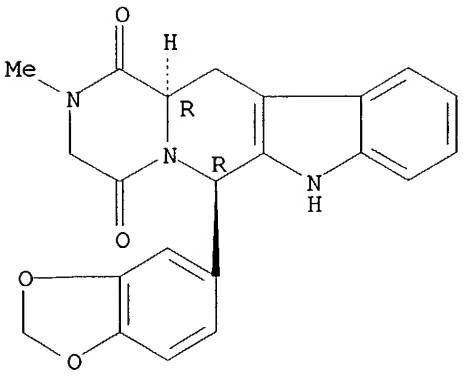
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003042216	A1	20030522	WO 2002-US35721	20021107
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SC, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VC, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003176413	A1	20030918	US 2002-290011	20021107
PRAI	US 2001-344498P	P	20011109		

OS MARPAT 138:401744
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [q = 0-2; R1, R3-6 = H, alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl; R2 = H, halo, alkyl, alkoxy, etc.; Y = alkyl, aryl] are prepd. For instance, 4-amino-1-benzyl-5-(ethoxycarbonyl)imidazole (prepn. given) is treated with ethylisocyanate (o-xylene, reflux, 16 h), the resulting product cyclized (MeOH, NaOMe, reflux, 4 h), subsequently treated with POCl3 and the product used to alkylate (R)-2-amino-3-phenylpropanol (NMP, 130.degree., 12 h) which provides II. II is treated with MsCl (Et3N), debenzylated (MeOH, NH4O2CH, Pd(OH)2/C, reflux, 3 h), brominated (HOAc, NaOAc, Br2), alkylated with 3-chloro-4-methoxybenzyl bromide (DMF, K2CO3) and treated with NaOEt (DMF/EtOH) to afford III. III has IC50 < 4.1 nM for PDE V and IC50 > 300 nM for PDE VI. I are useful for treating sexual dysfunction.
IT **171596-29-5**, IC-351
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; prepn. of polycyclic guanine deriv. phosphodiesterase V inhibitors)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

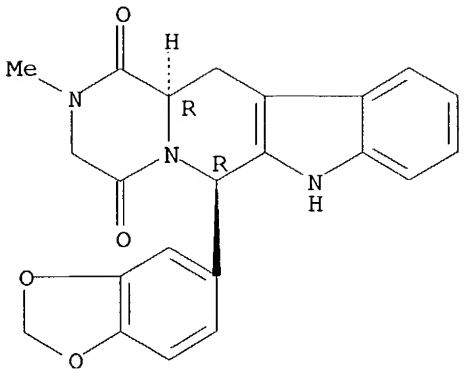
L5 ANSWER 17 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:319257 CAPLUS
DN 138:343856
TI Buccal sprays or capsules containing cardiovascular or renal drugs
IN Dugger, Harry A.
PA USA
SO U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 537,118.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003077229	A1	20030424	US 2002-230075	20020829
	WO 9916417	A1	19990408	WO 1997-US17899	19971001
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	EP 1029536	A1	20000823	EP 2000-109347	19971001
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	EP 1036561	A1	20000920	EP 2000-109357	19971001
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	WO 1997-US17899	A2	19971001		
	US 2000-537118	A2	20000329		
	EP 1997-911621	A3	19971001		

AB Buccal aerosol sprays or capsules using polar and non-polar solvent have now been developed which provide biol. active compds. for rapid absorption through the oral mucosa, resulting in fast onset of effect. The buccal polar compns. of the invention comprise formulation A: aq. polar solvent, active compd., and optional flavoring agent; formulation B: aq. polar solvent, active compd., optionally flavoring agent, and propellant; formulation C: non-polar solvent, active compd., and optional flavoring agent; and formulation D: non-polar solvent, active compd., optional flavoring agent, and propellant. Thus, a polar lingual spray contained isoproterenol-HCl 0.5-6, water 50-75, EtOH 5-10, PEG 5-15, sorbitol 0.4-1.0, aspartame 0.04-0.1, and flavors 2-3%.

IT **171596-29-5**, Tadalafil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(buccal sprays or capsules contg. cardiovascular or renal drugs)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).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L5 ANSWER 18 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:296061 CAPLUS
DN 138:297701
TI Transmucosal administration of phosphodiesterase inhibitors for the treatment of erectile dysfunction
IN Doherty, Paul C., Jr.; Place, Virgil A.; Smith, William L.
PA Vivus, Inc., USA
SO U.S., 13 pp., Cont.-in-part of U.S. 6,037,346.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7

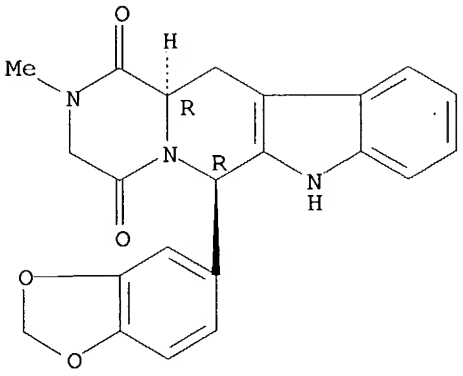
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6548490	B1	20030415	US 1999-467094	19991210
	US 6037346	A	20000314	US 1998-181070	19981027
	WO 2001041807	A2	20010614	WO 2000-US33372	20001208
	WO 2001041807	A3	20020214		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1237577	A2	20020911	EP 2000-986297	20001208
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003516363	T2	20030513	JP 2001-543151	20001208
	US 2002037828	A1	20020328	US 2001-888250	20010621
	US 6403597	B2	20020611		
	US 2002004498	A1	20020110	US 2001-938417	20010823
	US 2003134861	A1	20030717	US 2003-351198	20030124
PRAI	US 1997-958816	B2	19971028		
	US 1998-181070	A2	19981027		
	US 1999-467094	A	19991210		
	WO 2000-US33372	W	20001208		

AB A method is provided for treating erectile dysfunction in a mammalian male individual. The method involves the transmucosal administration of a phosphodiesterase inhibitor or a pharmaceutically acceptable salt, ester, amide or deriv. thereof, within the context of an effective dosing regimen. Preferred modes of administration include transbuccal, sublingual and transrectal routes. Pharmaceutical formulations and kits are provided as well.

IT **171596-29-5**, Tadalafil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transmucosal administration of phosphodiesterase inhibitors for the treatment of erectile dysfunction)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

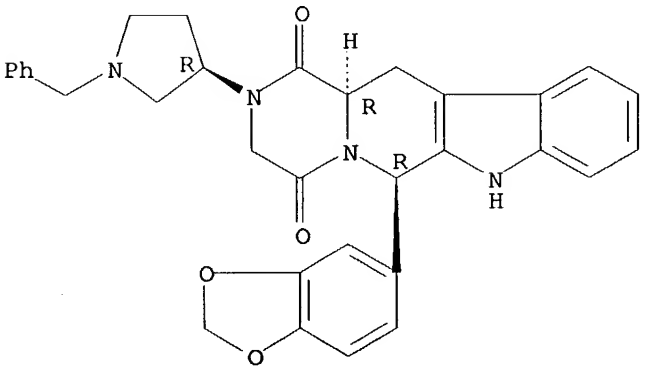
Absolute stereochemistry. Rotation (+).



RE.CNT 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 19 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:262948 CAPLUS
DN 139:159439
TI Design, synthesis and biological activity of .beta.-carboline-based type-5 phosphodiesterase inhibitors
AU Maw, Graham N.; Allerton, Charlotte M. N.; Gbekor, Eugene; Million, William A.
CS Pfizer Global Research and Development, Department of Discovery Chemistry, Sandwich Laboratories (IPC351), Sandwich, Kent, CT13 9NJ, UK
SO Bioorganic & Medicinal Chemistry Letters (2003), 13(8), 1425-1428
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science B.V.
DT Journal
LA English
OS CASREACT 139:159439
AB The SAR of a series of .beta.-carboline derived type 5 phosphodiesterase inhibitors has been explored and we have discovered compds. with excellent levels of PDE5 potency and selectivity over PDE6. However, the series exhibits low levels of selectivity over PDE11, a phosphodiesterase with unknown function.
IT **574730-01-1**
RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(design, synthesis and structure-activity relationship of .beta.-carboline-based type-5 phosphodiesterase inhibitors)
RN 574730-01-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(3R)-1-(phenylmethyl)-3-pyrrolidinyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



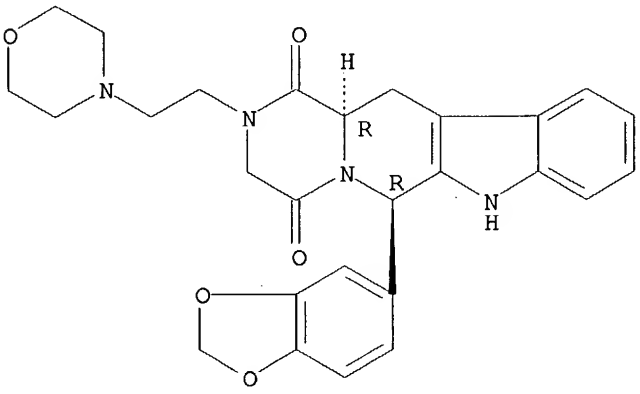
IT **385770-04-7P 574729-97-8P 574729-98-9P**
574729-99-0P 574730-00-0P 574730-03-3P
574730-04-4P 574730-05-5P 574730-06-6P
574730-07-7P 574730-08-8P 574730-09-9P
574730-10-2P 574730-11-3P 574730-12-4P
574730-13-5P 574730-14-6P 574730-15-7P
574730-16-8P 574730-17-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(design, synthesis and structure-activity relationship of

.beta.-carboline-based type-5 phosphodiesterase inhibitors)

RN 385770-04-7 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(4-morpholinyl)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

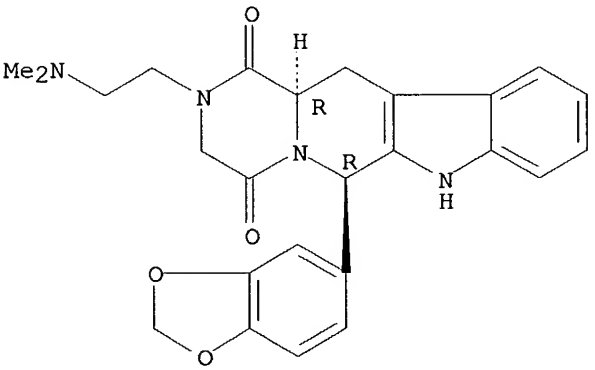
Absolute stereochemistry.



RN 574729-97-8 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-(dimethylamino)ethyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

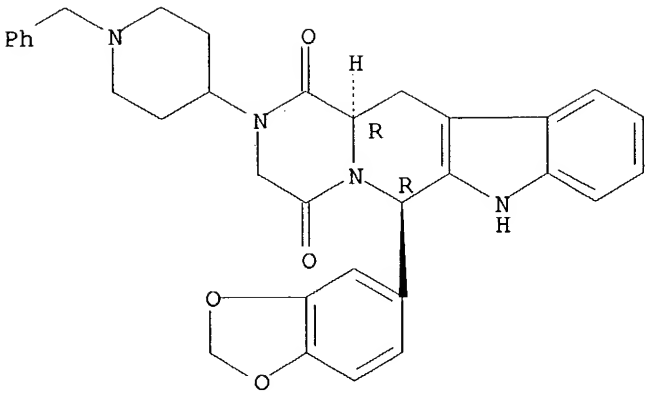
Absolute stereochemistry.



RN 574729-98-9 CAPLUS

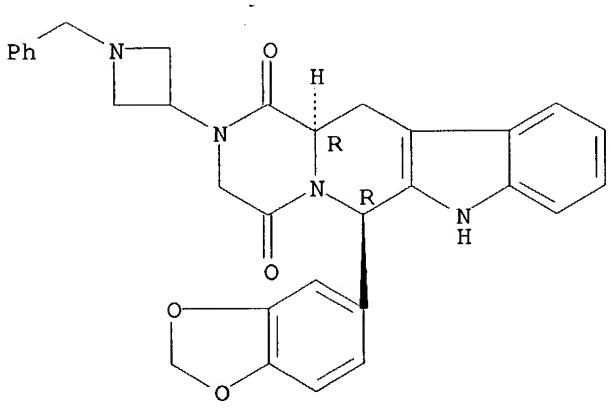
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[1-(phenylmethyl)-4-piperidinyl]-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



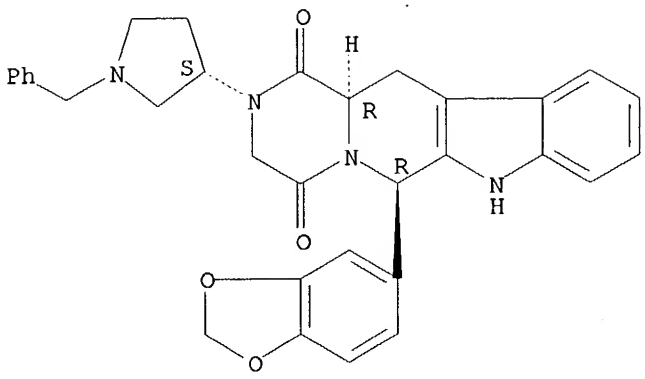
RN 574729-99-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[1-(phenylmethyl)-3-azetidinyl]-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



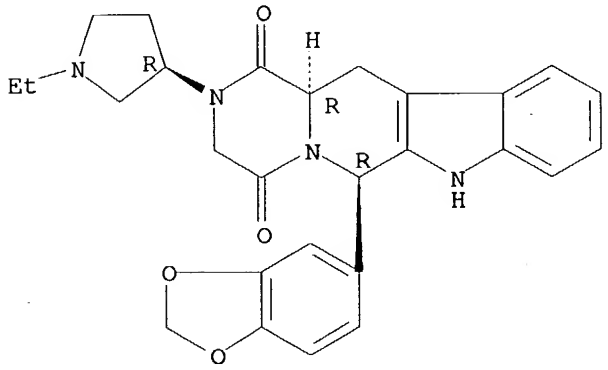
RN 574730-00-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(3S)-1-(phenylmethyl)-3-pyrrolidinyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



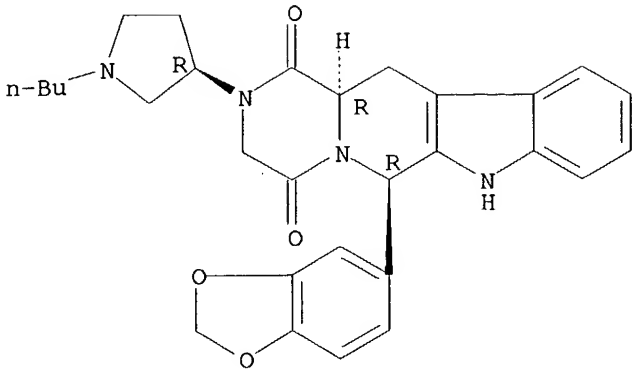
RN 574730-03-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[(3R)-1-ethyl-3-pyrrolidinyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



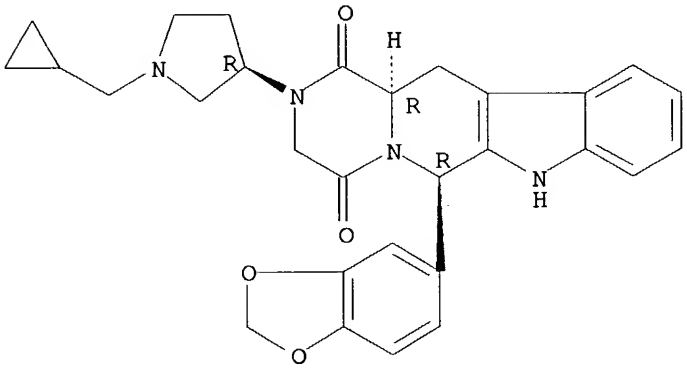
RN 574730-04-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[(3R)-1-butyl-3-pyrrolidinyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



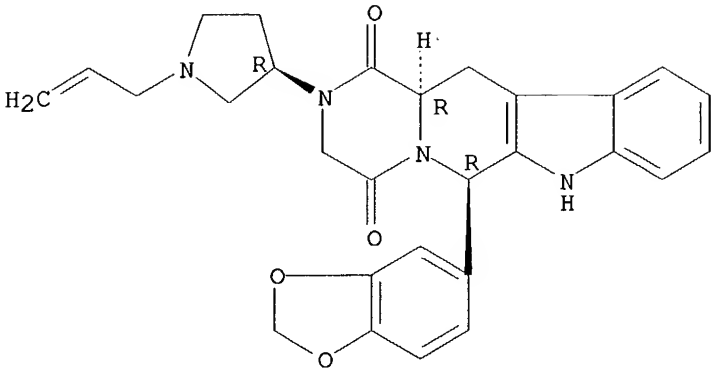
RN 574730-05-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[(3R)-1-(cyclopropylmethyl)-3-pyrrolidinyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



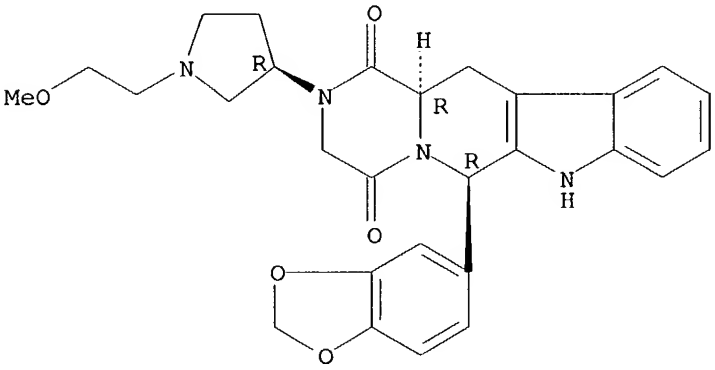
RN 574730-06-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(3R)-1-(2-propenyl)-3-pyrrolidinyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



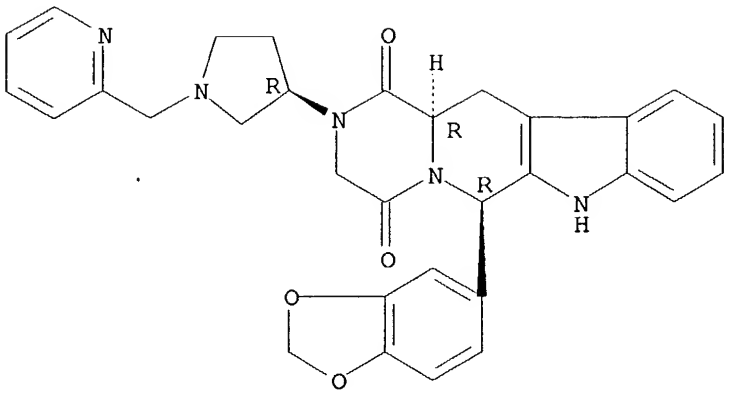
RN 574730-07-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(3R)-1-(2-methoxyethyl)-3-pyrrolidinyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



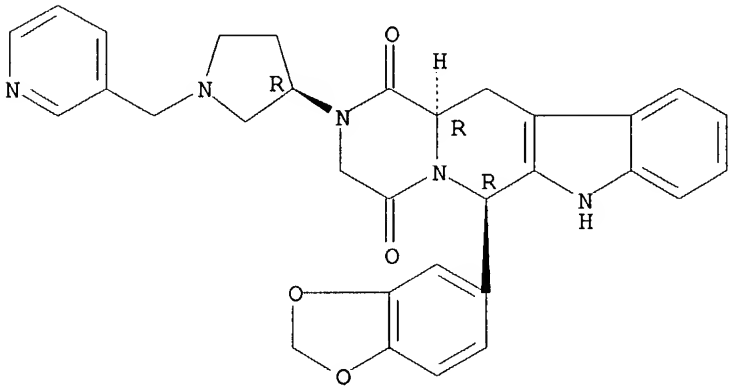
RN 574730-08-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(3R)-1-(2-pyridinylmethyl)-3-pyrrolidinyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



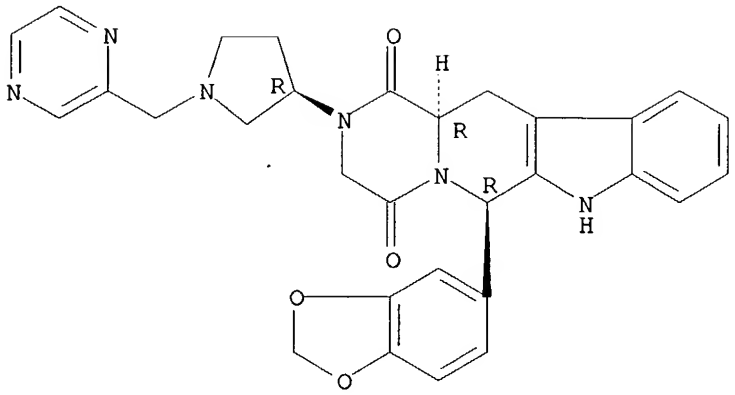
RN 574730-09-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(3R)-1-(3-pyridinylmethyl)-3-pyrrolidinyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



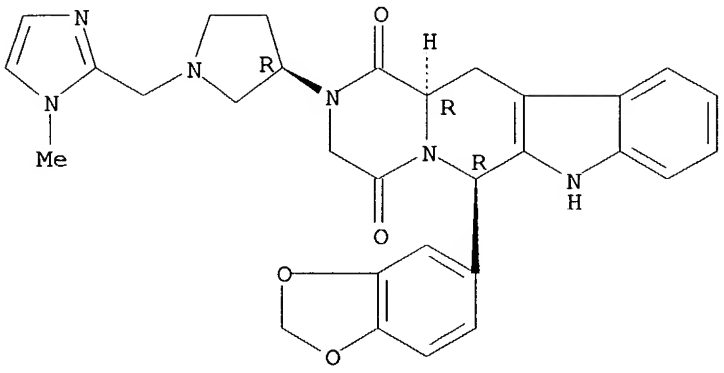
RN 574730-10-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(3R)-1-(pyrazinylmethyl)-3-pyrrolidinyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



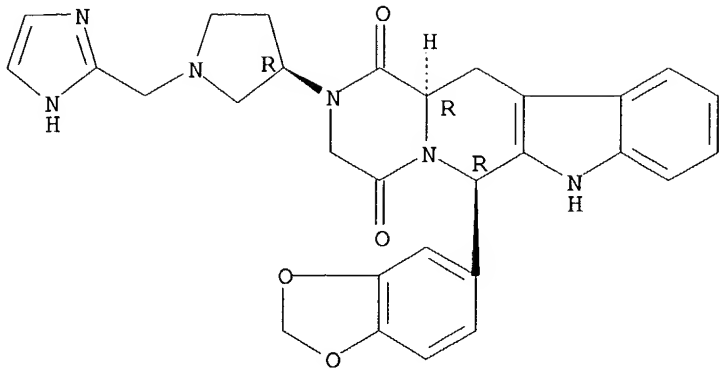
RN 574730-11-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(3R)-1-[(1-methyl-1H-imidazol-2-yl)methyl]-3-pyrrolidinyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



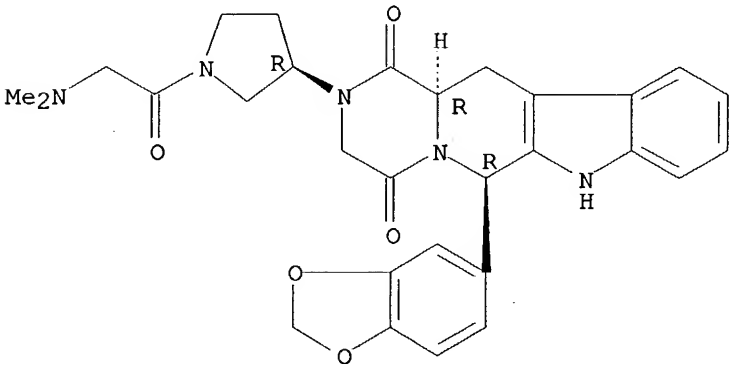
RN 574730-12-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(3R)-1-(1H-imidazol-2-ylmethyl)-3-pyrrolidinyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



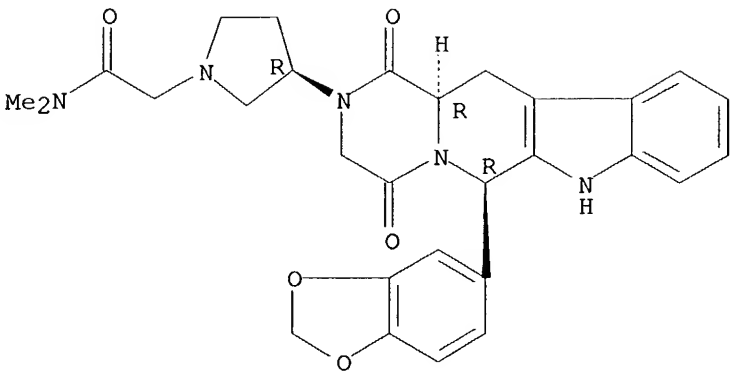
RN 574730-13-5 CAPLUS
CN Pyrrolidine, 3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]-1-[(dimethylamino)acetyl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



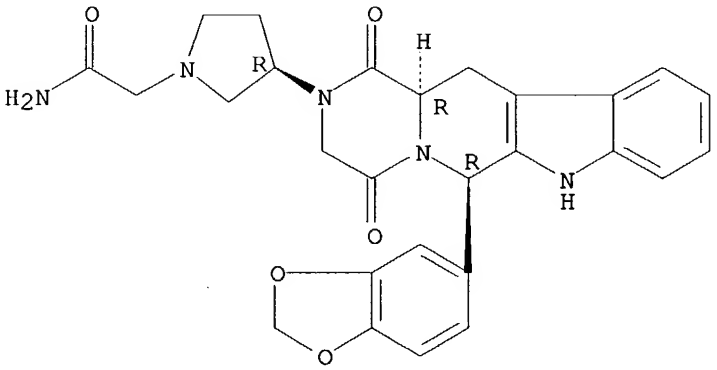
RN 574730-14-6 CAPLUS
CN 1-Pyrrolidineacetamide, 3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]-N,N-dimethyl-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



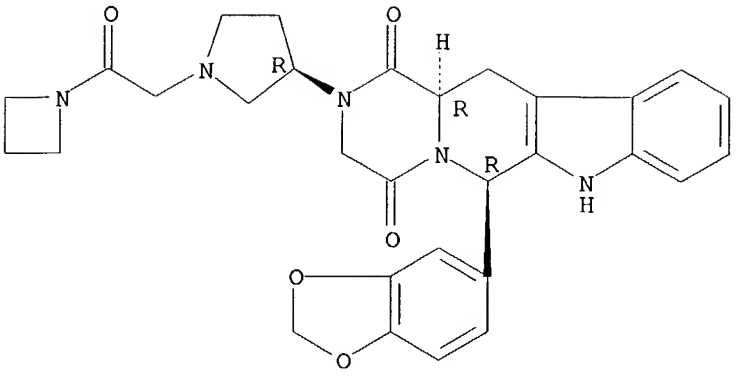
RN 574730-15-7 CAPLUS
CN 1-Pyrrolidineacetamide, 3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



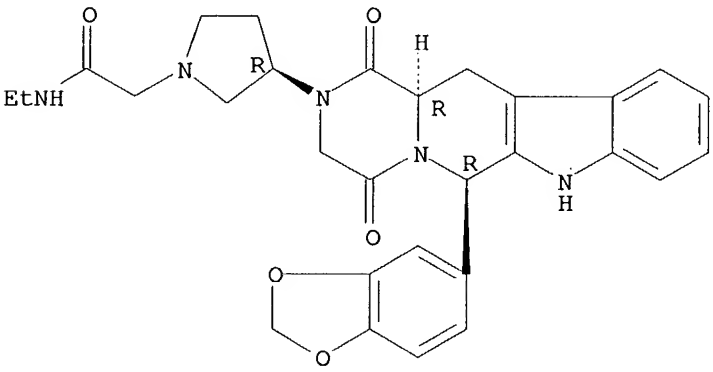
RN 574730-16-8 CAPLUS
CN Azetidine, 1-[[(3R)-3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]-1-pyrrolidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



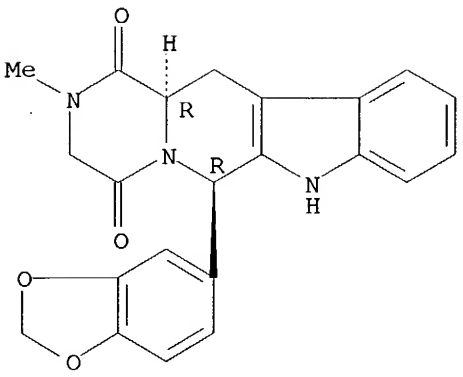
RN 574730-17-9 CAPLUS
CN 1-Pyrrolidineacetamide, 3-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]-N-ethyl-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



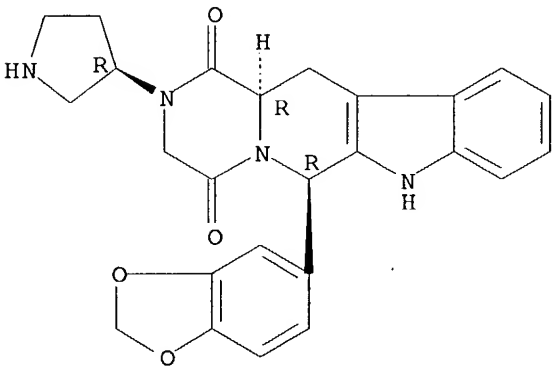
IT **171596-29-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(design, synthesis and structure-activity relationship of .beta.-carboline-based type-5 phosphodiesterase inhibitors)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



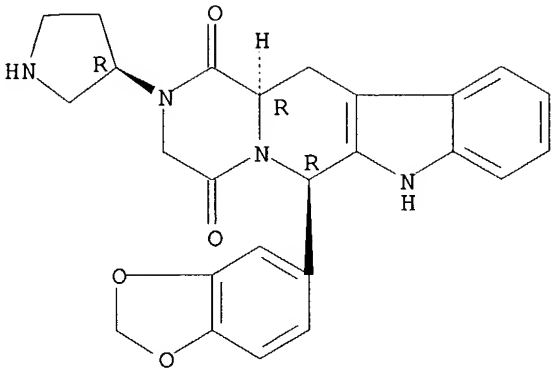
IT **574730-02-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design, synthesis and structure-activity relationship of .beta.-carboline-based type-5 phosphodiesterase inhibitors)
RN 574730-02-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(3R)-3-pyrrolidinyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **574730-02-2DP**, derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(design, synthesis and structure-activity relationship of .beta.-carboline-based type-5 phosphodiesterase inhibitors)
RN 574730-02-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(3R)-3-pyrrolidinyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

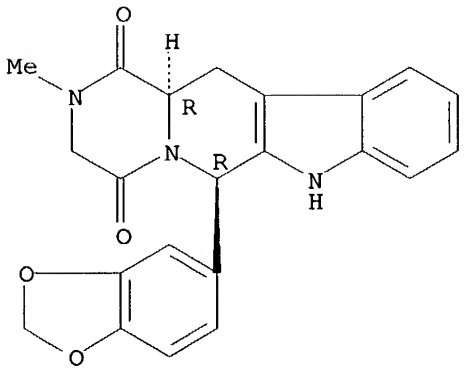
Absolute stereochemistry.



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:245950 CAPLUS
DN 138:395247
TI Tadalafil Lilly ICOS
AU Rotella, David P.
CS Hopewell Discovery Chemistry, Bristol-Myers Squibb Company, Princeton, NJ, 08543-5400, USA
SO Current Opinion in Investigational Drugs (Thomson Current Drugs) (2003), 4(1), 60-65
CODEN: COIDAZ; ISSN: 1472-4472
PB Thomson Current Drugs
DT Journal; General Review
LA English
AB A review. Tadalafil is a phosphodiesterase type 5 inhibitor in development by Lilly ICOS for the potential treatment of erectile dysfunction. The compd. will be marketed in North America and Europe by a collaboration formed by Eli Lilly & Co and ICOS Corp. Eli Lilly & Co has marketing rights in all other territories. Marketing approval in Europe was granted in Nov. 2002, with launch expected in the first half of 2003. An approvable letter was issued by the FDA in Apr. 2002, with a US launch anticipated in the first half of 2003.
IT **171596-29-5**, Cialis
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tadalafil (Cialis) for the potential treatment of erectile dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

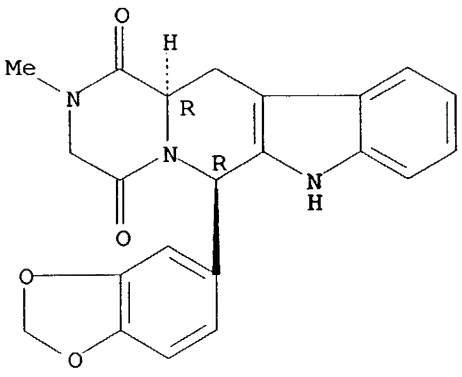
Absolute stereochemistry. Rotation (+).



RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:228126 CAPLUS
DN 138:379173
TI Erectile dysfunction in patients with diabetes mellitus - advances in treatment with phosphodiesterase type 5 inhibitors
AU Snow, Kenneth J.
CS Joslin Diabetes Cent., Boston, MA, 02215, USA
SO British Journal of Diabetes & Vascular Disease (2002), 2(4), 282-287
CODEN: BJDVAI; ISSN: 1474-6514
PB MediNews (Diabetes) Ltd.
DT Journal
LA English
AB In 4 independent, 12-wk, randomized, placebo-controlled clin. trials that evaluated the proerectile properties of the selective phosphodiesterase type 5 (PDE-5) inhibitors sildenafil (Viagra) (25-100 mg), tadalafil (10 and 20 mg) and vardenafil (10 and 20 mg) in men with erectile dysfunction (ED) secondary to diabetes mellitus, all the drugs were superior to placebo. In this difficult-to-treat population, the greatest difference from placebo for the overall responder rate of diabetic men reporting improved erections occurred with 20 mg vardenafil (72% vs. 13% for placebo). All the PDE-5 inhibitors were generally well tolerated. There were fewer reports of visual disturbance with vardenafil or tadalafil than with sildenafil, which may be due to their greater selectivity for PDE-5 inhibition and less cross-reactivity with retinal PDE-6 inhibition. The studies suggest there may be significant differences between the three drugs.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(erectile dysfunction in patients with diabetes mellitus treatment by the phosphodiesterase-5 inhibitors sildenafil, tadalafil, and vardenafil)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 22 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:221501 CAPLUS
DN 138:243313
TI Pharmaceutical composition comprising gamma-butyrobetaine for stimulating the sexual activity and potency
IN Kalvinsh, Ivars; Veveris, Maris; Birmans, Anatolijs
PA Latvia
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003022263	A1	20030320	WO 2002-LV5	20020304

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

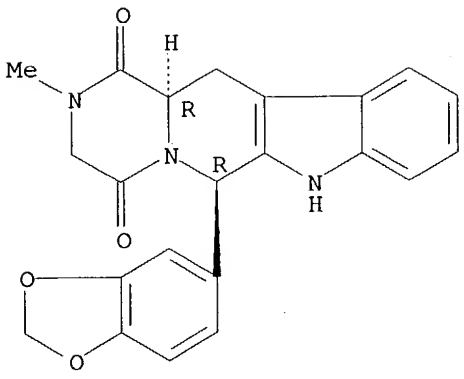
PRAI LV 2001-133 A 20010907

AB New medical use for gamma-butyrobetaine is disclosed. Also disclosed are pharmaceutical compns., contg. gamma-butyrobetaine or combination thereof with L-carnitine or sildenafil for oral, parenteral, s.c., transdermal, topical, sublingual, intrauetral, intranasal or rectal application, useful for stimulation of sexual activity and potency in mammals. The disclosed compns., when applied orally for 6 wk to non-narcotized male rats substantially increase their sexual activity, decreasing the arousal time, increasing the no. of copulations and resultativeness of mounting attempts. When applied by intracavernous or i.v. route said pharmaceutical compns. increase intracorporeal pressure and duration of erection, as well as restore stimulation-induced reflectory erections in anesthetized animals.

IT **171596-29-5**, Tadalafil
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Pharmaceutical compn. comprising gamma-butyrobetaine for stimulating the sexual activity and potency)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 23 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:221500 CAPLUS
DN 138:231752
TI Sexual activity stimulating composition comprising .gamma.-butyrobetaine
IN Kalvinsh, Ivars; Veveris, Maris; Birmans, Anatolijs
PA Latvia
SO PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003022262	A1	20030320	WO 2002-LV4	20020304

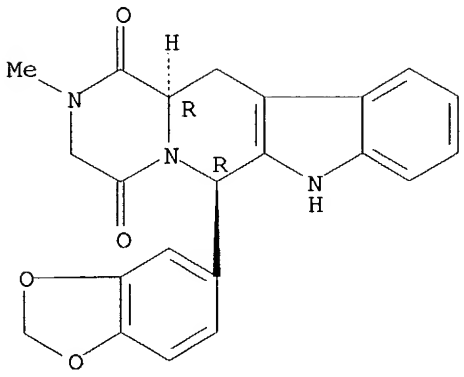
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI LV 2001-134 A 20010907

AB Disclosed are pharmaceutical compns., contg. .gamma.-butyrobetaine or combination with 3-(2,2,2-trimethylhydrazinium)propionate or sildenafil for oral, parenteral, s.c., transdermal, topical, sublingual, intrauretral, intranasal or rectal application, useful for stimulation of sexual activity and potency in mammals. The disclosed compns., when applied orally for 6 wk to non-narcotized male rats substantially increase their sexual activity, decreasing the arousal time, increasing the no. of copulations and mounting attempts. When applied by intracavernous or i.v. route said pharmaceutical compns. increase intracorporeal pressure and duration of erection, as well as restore stimulation-induced reflectory erection in narcotized animals.

IT **171596-29-5**, Tadalafil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sexual activity stimulating compn. comprising .gamma.-butyrobetaine)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

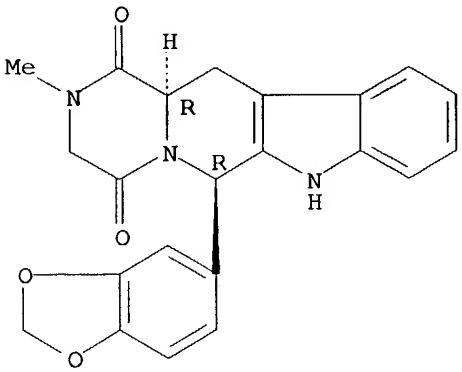
Absolute stereochemistry. Rotation (+).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 24 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:108230 CAPLUS
DN 138:198494
TI Tadalafil phase 3 experience
AU Stuckey, Bronwyn G. A.
CS Department of Endocrinology and Diabetes, Keogh Institute for Medical Research, Sir Charles Gairdner Hospital, Nedlands, 6009, Australia
SO European Urology, Supplements (2002), 1(8), 25-30
CODEN: EUSUAU; ISSN: 1569-9056
PB Elsevier Science B.V.
DT Journal
LA English
AB Objectives: To evaluate the efficacy and safety of tadalafil, a potent, oral phosphodiesterase type 5 inhibitor for erectile dysfunction. Methods: Integrated analyses of five 12-wk, randomized, double-blind, placebo-controlled phase 3 clin. trials involving 1112 men with mild-to-severe erectile dysfunction of various etiologies taking as-needed tadalafil 2.5, 5, 10 or 20 mg (n = 804) or placebo (n = 308) were conducted. Results: Tadalafil therapy significantly enhanced erectile function (vs. placebo), eliciting robust changes that were consistent across a no. of efficacy outcome measures. Ratings of erectile function, the likelihood of successfully completing intercourse, and proportions of men reporting enhanced erectile function were significantly higher in tadalafil patients compared with placebo controls. Eighty-one percent of all men who were treated with tadalafil 20 mg reported improved erections at study endpoint compared with 35% of placebo controls. Tadalafil was well tolerated, with headache and dyspepsia being the most frequent treatment-emergent adverse events. These events tended to be mild or moderate and to abate with continued dosing. Conclusions: Tadalafil therapy significantly ameliorated erectile function and was well tolerated by a broad spectrum of men with erectile insufficiency.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tadalafil for erectile dysfunction patients)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

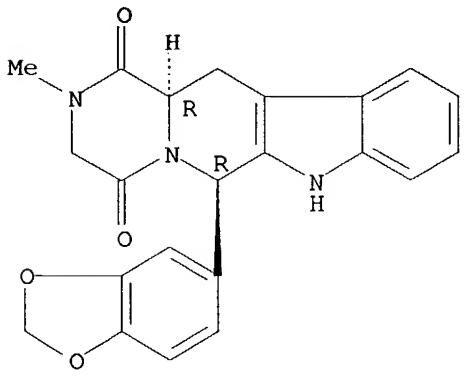
Absolute stereochemistry. Rotation (+).



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 25 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:108228 CAPLUS
DN 138:198051
TI Restoring a normal sexual response: the ultimate goal of erectile dysfunction therapy
AU Porst, Hartmut
CS Private Urological Practice, Hamburg, D-20345, Germany
SO European Urology, Supplements (2002), 1(8), 19-24
CODEN: EUSUAU; ISSN: 1569-9056
PB Elsevier Science B.V.
DT Journal; General Review
LA English
AB A review. Erectile dysfunction may compromise quality of life for more than 30 million European men (and their partners). Although more likely with advancing age, erectile insufficiency can be effectively and safely treated and is no longer considered an inevitable consequence of aging. One potential treatment, the investigational agent tadalafil, is a potent, selective, reversible inhibitor of phosphodiesterase type 5 with a favorable pharmacokinetic profile that may translate into practical advantages. These advantages include a broad window of therapeutic responsiveness, which may relieve some men of the pressure to perform within a specific time frame and reduce the amt. of planning of sexual activity. Plasma tadalafil concns. are not affected by age, comorbidities (e.g. diabetes), food or alc. This profile should render treatment regimens convenient and uncomplicated, with consistent, "real-world" efficacy in a broad patient spectrum. In randomized, double-blind, placebo-controlled studies tadalafil, taken as needed before sexual activity without restrictions on food/alc. intake, significantly enhanced erectile function (vs. placebo), leading to successful intercourse in over 70% of attempts at more than 30 min to 24 h after dosing and approx. 60% at 36 h. Tadalafil was well tolerated; headache and dyspepsia were the most common treatment-emergent adverse effects.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(restoring normal sexual response as ultimate goal of therapy for erectile dysfunction patients)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



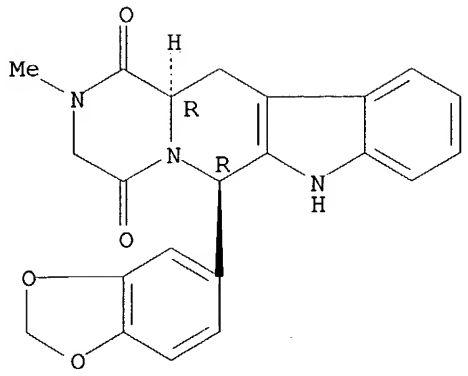
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 26 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:42146 CAPLUS
DN 138:83422
TI Use of 2,5-dihydroxybenzenesulfonic acid derivatives in the production of a medicament used to potentiate the effect of other drugs in the treatment of erectile dysfunction
IN Esteve-Soler, Jose; Tejada-Gorman, Inigo De Saenz
PA Laboratorios del Esteve, S.A., Spain
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA Spanish
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003004097	A1	20030116	WO 2002-ES325	20020701
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	ES 2180446	A1	20030201	ES 2001-1535	20010702
PRAI	ES 2001-1535	A	20010702		

AB The invention relates to the use of 2,5-dihydroxybenzenesulfonic acid derivs. in the prodn. of medicaments that are used in therapeutics in order to potentiate the effects of inhibitors of phosphodiesterase-5 including sildenafil, vardenafil and IC-351, apomorphine, nitric oxide including amyl nitrate, nitroglycerin, nitroprusside, nitrosothiol and nicorandil, compds. that increase the cyclic GMP level in the penile tissue and other compds. that are intended to stimulate penile erection in men.
IT **171596-29-5**, Ic-351
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of 2,5-dihydroxybenzenesulfonic acid derivs. to potentiate the effect of other drugs in the treatment of erectile dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

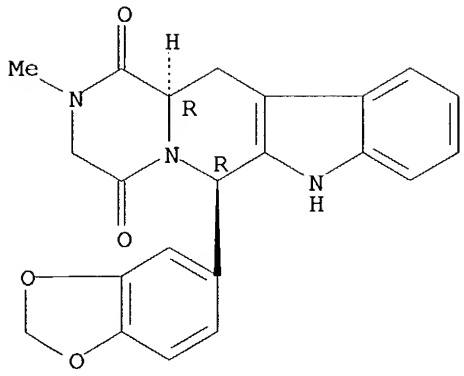
Absolute stereochemistry. Rotation (+).



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 27 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:9502 CAPLUS
DN 138:49292
TI Erectile dysfunction: comparison of efficacy and side effects of the PDE-5 inhibitors sildenafil, vardenafil and tadalafil review of the literature
AU Gresser, U.; Gleiter, C. H.
CS Internal Medicine, Praxisklinik Sauerlach, Germany
SO European Journal of Medical Research (2002), 7(10), 435-446
CODEN: EJMRFL; ISSN: 0949-2321
PB I. Holzapfel Publishers
DT Journal; General Review
LA English
AB A review. Since introduction of the PDE-5 inhibitor sildenafil 4 yr ago, there has been a fundamental change in the treatment of erectile dysfunction (ED). Intracavernosal or intraurethral injections of vasoactive substances or penile implants as mech. aids now play hardly any part in it. The development of the PDE-5 inhibitors vardenafil and tadalafil prompts the question of whether and how these three substances differ in terms of their efficacy and adverse effects. Sildenafil has proven to be a very effective medicinal product. Studies with a follow-up period of up to 6 yr have been conducted. The success rate of sildenafil varies in the group of ED patients with an org. underlying disease from 43% in patients who have undergone radical prostatectomy to 85% in patients with a neurol. underlying disease, and amts. to an av. 82% (range 43-85%, 100mg). In an evaluation of spontaneous reports of deaths assocd. with sildenafil, the FDA concluded that there was no deducible evidence of an increase in the mortality rate among sildenafil users compared to the general population. In fact, fewer deaths assocd. in time with the ingestion of sildenafil were reported than might have been expected purely statistically on the basis of the normal mortality rate for men in this age group. According to the initial studies conducted, vardenafil and tadalafil demonstrate efficacy data approx., comparable to those of sildenafil. As yet, insufficient data are available to evaluate the adverse effects of vardenafil and tadalafil, particularly their long-term use and use in high-risk groups. Sildenafil has already been used by over 20 million men in over 110 countries and is one of the best-studied pharmacol. substances available. This advantage in terms of knowledge and safety data makes sildenafil a safe and reliable treatment for patients with erectile dysfunction.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of efficacy and side effects of PDE-5 inhibitors sildenafil, vardenafil and tadalafil for patients with erectile dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

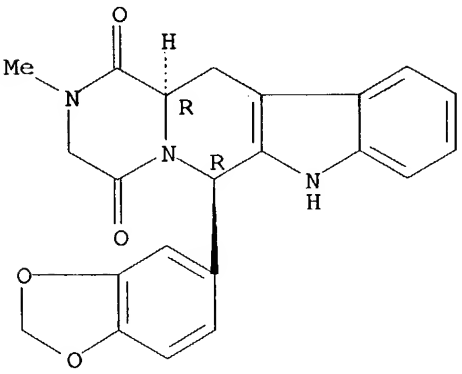
Absolute stereochemistry. Rotation (+).



RE.CNT 92 THERE ARE 92 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 28 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:968677 CAPLUS
DN 138:32694
TI Overview of the cardiovascular effects of tadalafil
AU Emmick, J. T.; Stuewe, S. R.; Mitchell, M.
CS Eli Lilly and Company, Indianapolis, IN, USA
SO European Heart Journal Supplements (2002), 4(Suppl. H), H32-H47
CODEN: EHJSFT; ISSN: 1520-765X
PB W. B. Saunders
DT Journal; General Review
LA English
AB A review. Because erectile dysfunction (ED) and cardiovascular disease share a no. of risk factors, it is important to understand the hemodynamic and cardiovascular effects of treatments for ED, including the phosphodiesterase (PDE) type 5 inhibitors. In healthy subjects, administration of tadalafil (a potent and selective inhibitor of PDE5 indicated for the treatment of ED) resulted in small decreases in standing blood pressure. In the general population of men with ED, the effects of tadalafil on hemodynamic parameters were similar to those obsd. with placebo. As with sildenafil, administration of tadalafil with any nitrate is contraindicated. Tadalafil administration was not assocd. with prolongation in QT interval. Safety data show that the incidence rate of myocardial infarction following treatment with tadalafil was comparable to that obsd. in the age-standardized male population, and incidence rates of cardiovascular events obsd. in patients who were and were not treated with concomitant antihypertensive therapy were comparable. These results demonstrate that tadalafil has no clin. relevant effects on hemodynamics, although it should not be used in combination with nitrates. In addn., integrated analyses of the cardiovascular adverse events in the phase III safety database as a whole, and in patients taking concomitant antihypertensive medication, demonstrate that tadalafil is not assocd. with increased risk for clin. significant cardiovascular events.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cardiovascular effects of tadalafil)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

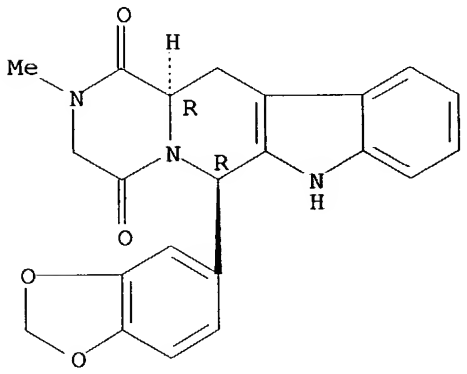


RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 29 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:968676 CAPLUS
DN 138:32693
TI Tadalafil: a novel treatment for erectile dysfunction
AU Giuliano, F.; Varanese, L.
CS Department of Urology, AP-HP, Centre Hospitalier Universitaire de Bicetre, Le Kremlin-Bicetre, Fr.
SO European Heart Journal Supplements (2002), 4(Suppl. H), H24-H31
CODEN: EHJSFT; ISSN: 1520-765X
PB W. B. Saunders
DT Journal; General Review
LA English
AB A review. Tadalafil, a potent, selective and reversible inhibitor of phosphodiesterase type 5 that is under review as an oral therapy for erectile dysfunction, has a time to max. concn. of 2 h and a half-life of 17.5 h. Systemic tadalafil exposure was not clin. significantly altered by age or diabetes. Food did not alter the rate and extent of absorption of tadalafil, and no restrictions regarding food or alc. intake were imposed on patients in tadalafil clin. trials. Furthermore, the time of dosing had no significant effect on the systemic distribution of tadalafil. Integrated analyses of data from five phase III trials demonstrated that tadalafil at doses from 5 mg to 20 mg significantly improved erectile function (vs placebo) by all efficacy measures. Tadalafil was safe and well tolerated in the phase III studies, with headache and dyspepsia being the most frequent adverse events. Addnl., in a sep. study of patients with erectile dysfunction and diabetes, tadalafil 10 mg and 20 mg significantly improved all efficacy measures as compared with placebo.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tadalafil as novel treatment for erectile dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

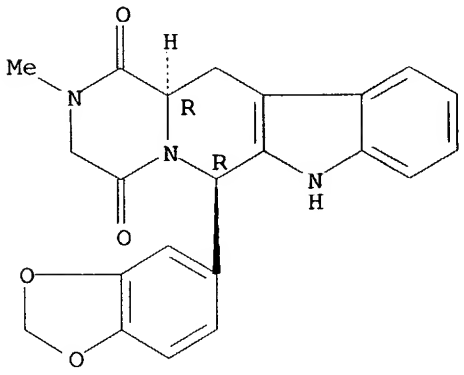
Absolute stereochemistry. Rotation (+).



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 30 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:968674 CAPLUS
DN 138:32691
TI Phosphodiesterase type 5 inhibition in erectile dysfunction: an overview
AU Giuliano, F.
CS Department of Urology, Centre Hospitalier Universitaire de Bicetre, Le Kremlin-Bicetre, Fr.
SO European Heart Journal Supplements (2002), 4(Suppl. H), H7-H12
CODEN: EHJSFT; ISSN: 1520-765X
PB W. B. Saunders
DT Journal; General Review
LA English
AB A review. Widely distributed throughout the body, cyclic nucleotide phosphodiesterases (PDEs) are functionally heterogeneous enzymes with potential roles in a no. of physiol. actions. Among these enzymes, PDE type 5 has received particular attention because of the widespread use of the PDE5 inhibitor sildenafil citrate as an oral therapy for erectile dysfunction. Within the corpus cavemosum of the penis, PDE5 catalyzes the enzymic degrdn. (inactivation) of cyclic 3',5'-guanosine monophosphate, which is a second messenger and key mediator of vascular and trabecular erectile tissue smooth muscle relaxation. By amplifying the nitric oxide-cyclic nucleotide signalling pathway, PDE5 inhibitors serve as 'contingent agonists' of the physiol. response to sexual arousal. In exptl. models, tadalafil increased the sensitivity of penile resistance arteries and erectile tissues to three stimuli of smooth muscle relaxation, namely elec. field stimulation, sodium nitroprusside, and acetylcholine. In randomized, double-blind, placebo-controlled trials, sildenafil and the investigational agents tadalafil and vardenafil significantly enhanced erectile function in the majority of patients and were well tolerated.
IT **171596-29-5**, Tadalafil
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase type 5 inhibition in erectile dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

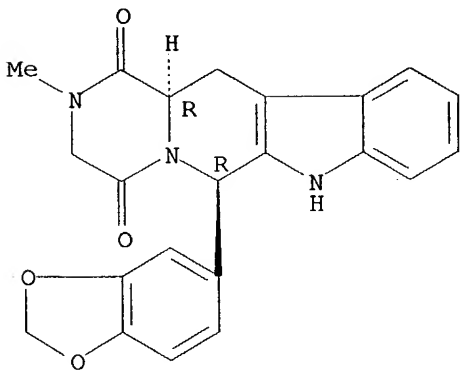
Absolute stereochemistry. Rotation (+).



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 31 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:966707 CAPLUS
DN 138:19445
TI Effects of tadalafil on erectile dysfunction in men with diabetes
AU De Tejada, Inigo Saenz; Anglin, Greg; Knight, James R.; Emmick, Jeffrey T.
CS Fundacion para la Investigacion y el Desarrollo en Andrologia, Madrid, Spain
SO Diabetes Care (2002), 25(12), 2159-2164
CODEN: DICAD2; ISSN: 0149-5992
PB American Diabetes Association, Inc.
DT Journal
LA English
AB The aim of this study was to evaluate the efficacy and safety of tadalafil taken as needed before sexual activity by men with diabetes and erectile dysfunction (ED). Men with type 1 or type 2 diabetes and a min. 3-mo history of ED were randomly allocated to one of three groups: placebo (n = 71), tadalafil 10 mg (n = 73), or tadalafil 20 mg (n = 72) taken up to once daily for 12 wk. Changes from baseline in mean scores on the erectile function domain of the International Index of Erectile Function (IIEF) and changes from baseline in the proportion of "yes" responses to question 2, "Were you able to penetrate," and 3, "Were you able to complete intercourse," of the Sexual Encounter Profile were coprimary outcome measures. A total of 191 (88%) of 216 patients completed the study. Treatment with tadalafil significantly improved all primary efficacy variables, regardless of baseline HbA1c level. Therapy with tadalafil also significantly improved a no. of secondary outcome measures, including changes in other IIEF domains, individual IIEF questions, and percentage of pos. responses to a global assessment question measuring erection improvement. Treatment with tadalafil did not alter mean HbA1c levels. Tadalafil was well tolerated, with headache and dyspepsia being the most frequent adverse events with active treatment. Tadalafil therapy significantly enhanced erectile function and was well tolerated by men with diabetes and ED.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of tadalafil on erectile dysfunction in men with diabetes)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



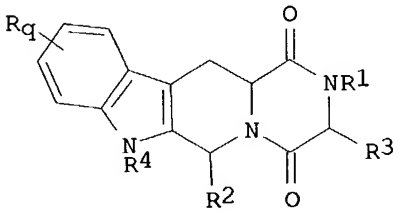
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 32 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:946286 CAPLUS
DN 138:24730
TI Preparation of pyrazinopyridoindolediones as phosphodiesterase 5 (PDE5) inhibitors.
IN Orme, Mark W.; Sawyer, Jason Scott; Schultze, Lisa M.
PA Lilly Icos LLC, USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098877	A1	20021212	WO 2002-US11791	20020415

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-296023P P 20010605
OS MARPAT 138:24730
GI



I

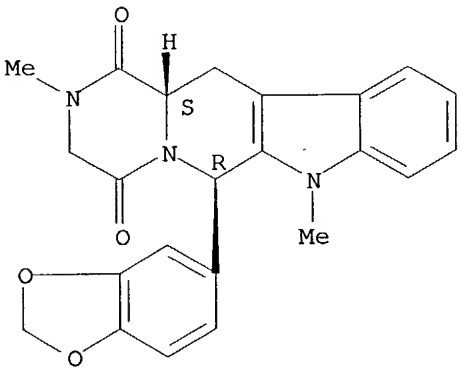
AB Title compds. [I; R = halo, alkyl; R1 = H, alkenyl, alkynyl, haloalkyl, cycloalkyl, (cyclo)alkylalkyl, aralkyl, heteroarylalkyl, etc.; R2 = (substituted) Ph, thienyl, furyl, pyridyl, benzo-fused 5-6 membered ring; R3 = H, alkyl; R1R3 = 3-4 membered alkyl, alkenyl; R4 = H, (cyclo)alkyl, heterocycloalkyl, alkenyl, alkylenearyl, aralkyl, CORa, aryl, heteroaryl, CORa, CONRaRb, CSNRaRb, SO2Ra, SO2NRaRb, SORa, SONRaRb, alkylenearyl, etc. substituted with .gtoreq.1 of SO2NRaRb, NRaRb, CO2Ra, NRaSO2CF3, CN, NO2, CORa, ORa, etc.; Q = O, S, NRa; Het = 5-6 membered (un)satd. heterocyclyl contg. .gtoreq.1 O, N, S, and optionally substituted with alkyl, CO2Ra; Ra = H, alkyl, aralkyl, alkylenearyl, (hetero)aryl, heteroarylalkyl, alkyleneheteroaryl; Rb = H, alkyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkyleneN(Ra)2, alkylenearyl, alkyleneHet, haloalkyl, (hetero)cycloalkyl, alkyleneheteroaryl, alkyleneCO2Ra, alkyleneheterocycloalkyl; RaRb = 5-6 membered ring optionally contg. .gtoreq.1 heteroatom; q = 0-4], were prepd. Thus, (6R,12aR)-7-acetyl-6-benzo[1,3]dioxol-5-yl-2-methyl-2,3,6,7,12,12a-hexahydropyrazino-[1',2':1,6]pyrido[3,4-b]indole-1,4-dione (prepn. given) inhibited PDE5

with IC50 = 0.007 .mu.M.

IT **477970-20-0P 477970-21-1P 477970-22-2P 477970-23-3P 477970-24-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compd.; prepn. of pyrazinopyridoindolediones as phosphodiesterase 5 (PDE5) inhibitors)

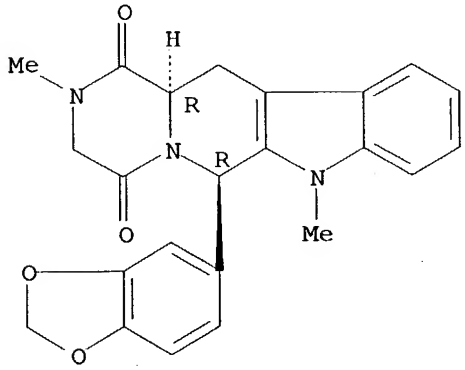
RN 477970-20-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,7-dimethyl-, (6R,12aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



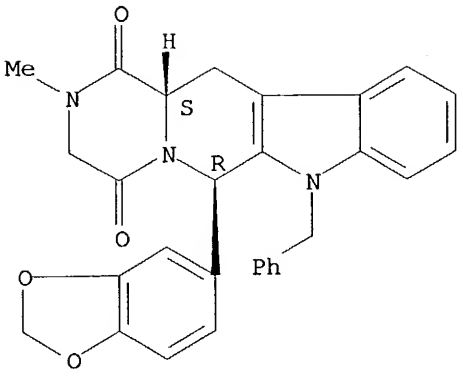
RN 477970-21-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,7-dimethyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



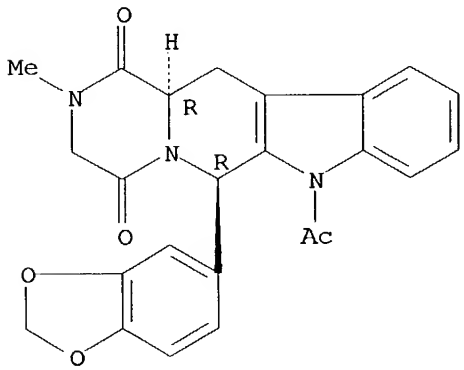
RN 477970-22-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-7-(phenylmethyl)-, (6R,12aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



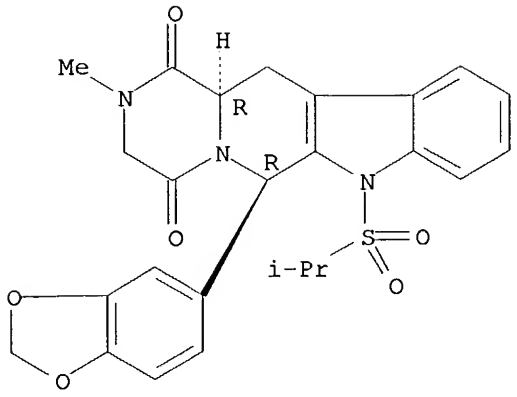
RN 477970-23-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 7-acetyl-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



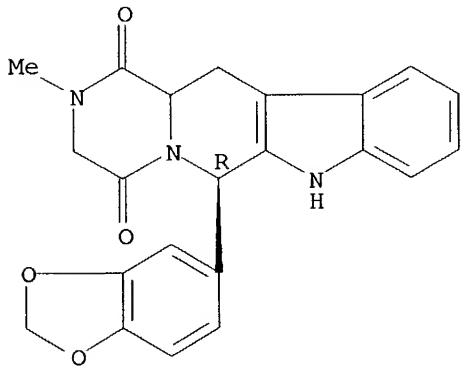
RN 477970-24-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-7-[(1-methylethyl)sulfonyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **378788-17-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pyrazinopyridoindolediones as phosphodiesterase 5 (PDE5) inhibitors)
RN 378788-17-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

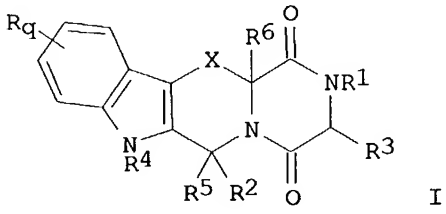
L5 ANSWER 33 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:946116 CAPLUS
DN 138:24726
TI Preparation of pyrazinopyridoindolediones and related compounds as phosphodiesterase 5 (PDE5) inhibitors
IN Orme, Mark W.; Sawyer, Jason Scott; Schultze, Lisa M.
PA Lilly Icos LLC, USA
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002098428	A1	20021212	WO 2002-US13703	20020502

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-296041P P 20010605
OS MARPAT 138:24726
GI



I

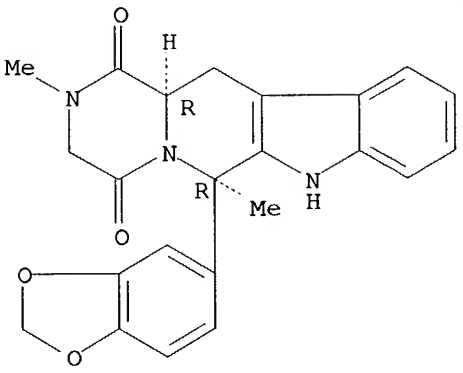
AB Title compds. [I; R = halo, alkyl; R1 = H, alkenyl, alkynyl, haloalkyl, cycloalkyl, (cyclo)alkylalkyl, aralkyl, heteroarylalkyl; R2 = (substituted) Ph, thienyl, furyl, pyridyl, benzo-fused 5-6 membered ring; R3 = H, alkyl; R1R3 = 3-4 membered alkyl, alkenyl chain; R4 = H, (cyclo)alkyl, heterocycloalkyl, alkenyl, alkylenearyl, aralkyl, CORa, aryl, heteroaryl, CORa, CONRaRb, CSNRaRb, SO2Ra, SO2NRaRb, SORa, SONRaRb, alkylenearyl, etc. substituted with .gtoreq.1 of SO2NRaRb, NRaRb, CO2Ra, NRaSO2CF3, CN, NO2, CORa, ORa, etc.; R5 = H, ORa, alkyl, (hetero)aryl, aralkyl, alkylenearyl, alkyleneHet, cycloalkyl, heterocycloalkyl; R6 = H, alkyl, (hetero)cycloalkyl, aryl, heteroaryl, ORa, CO2Ra, CORa, CONRaRb, CSORa, CSNRaRb; X = CHR7, CHR7CH2, CR7:CH, QCHR7, bond; Q = O, S, NRa; R7 = H, ORa, alkyl, (hetero)cycloalkyl, (hetero)aryl, alkylenearyl, alkyleneheteroaryl, alkyleneHet, arylalkyl, heteroarylalkyl; Het = 5-6 membered (un)satd. heterocyclyl contg. .gtoreq.1 O, N, S, and optionally substituted with alkyl, CO2Ra; Ra = H, alkyl, aralkyl, alkylenearyl, (hetero)aryl, heteroarylalkyl, alkyleneheteroaryl; Rb = H, alkyl, aryl, heteroaryl, aralkyl, heteroarylalkyl, alkyleneN(Ra)2, alkylenearyl,

alkyleneHet, haloalkyl, (hetero)cycloalkyl, alkyleneheteroaryl, alkyleneCO2Ra, alkyleneheterocycloalkyl; RaRb = 5-6 membered ring optionally contg. .gtoreq.1 heteroatom; q = 0-4; if X = CHR7, then .gtoreq.1 of R4, R5, R6, R7 .noteq. H], were prepd. Thus, (+-)-cis,trans-methyl-6-benzo[1,3]dioxol-5-yl-2,12-dimethyl-2,3,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-1,3-dione (prepn. from indole given) inhibited PDE5 with IC50 = 0.004 .mu.M.

IT **477978-85-1P 477978-89-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compd.; prepn. of pyrazinopyridoindolediones and related compds. as phosphodiesterase 5 (PDE5) inhibitors)

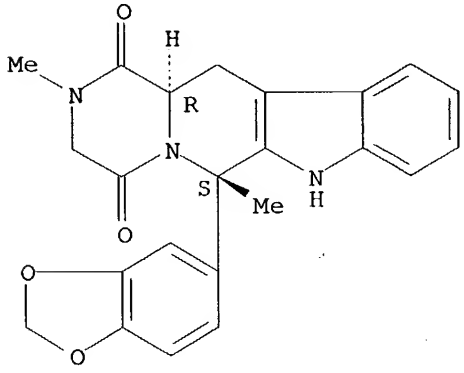
RN 477978-85-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,6-dimethyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 477978-89-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,6-dimethyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

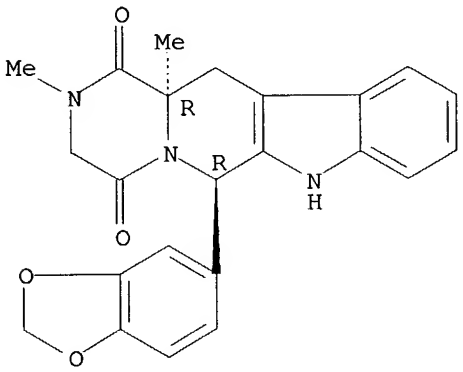


IT **477978-84-0P 477978-88-4P 477978-90-8P**

477979-09-2P 477979-10-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrazinopyridoindolediones and related compds. as phosphodiesterase 5 (PDE5) inhibitors)

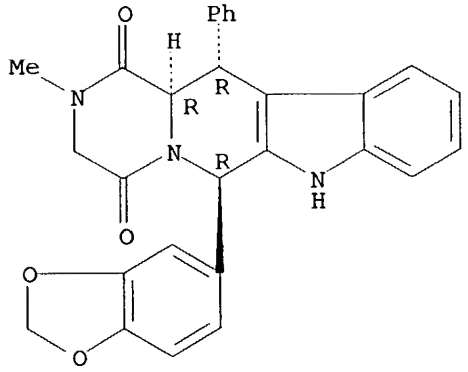
RN 477978-84-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,12a-dimethyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



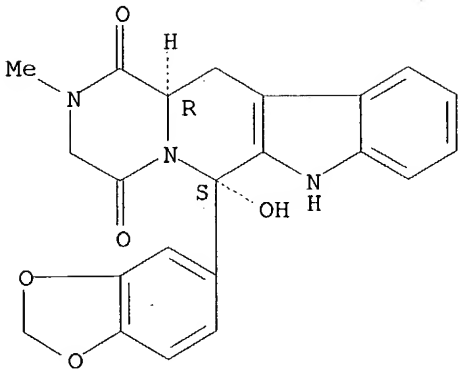
RN 477978-88-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-12-phenyl-, (6R,12R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



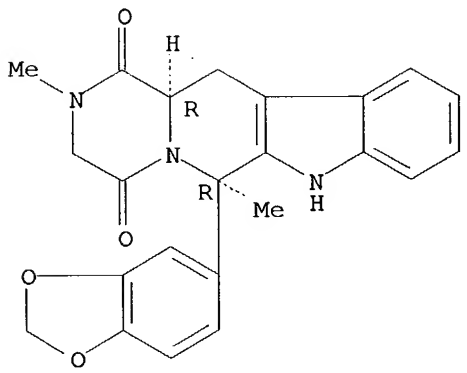
RN 477978-90-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-6-hydroxy-2-methyl-, (6S,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



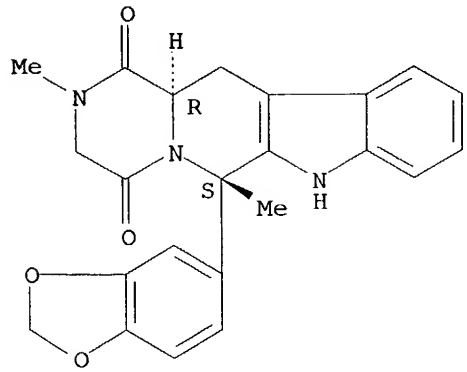
RN 477979-09-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,6-dimethyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 477979-10-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,6-dimethyl-, (6S,12aR)- (9CI) (CA INDEX NAME)

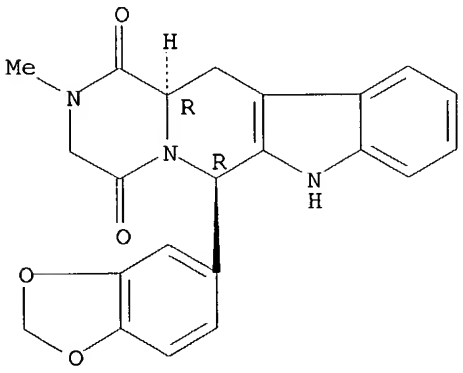
Absolute stereochemistry. Rotation (+).



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 34 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:926946 CAPLUS
DN 139:172867
TI Erectile dysfunction: current concepts and future directions
AU Monga, M.; Rajasekaran, M.
CS Department of Urologic Surgery, University of Minnesota, Minneapolis, MN, USA
SO Archives of Andrology (2003), 49(1), 7-17
CODEN: ARANDR; ISSN: 0148-5016
PB Taylor & Francis Inc.
DT Journal; General Review
LA English
AB A review. Major advances in science and medicine have led to improved understanding of the pathophysiol. of erectile dysfunction. The development of reliable pharmacol. therapy for erectile dysfunction has led to heightened awareness in the public and medical communities. This article reviews recent clin. advances and future research directions.
IT **171596-29-5,** Tadalafil
RL: BSU (Biological study, unclassified); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pathophysiol. and therapeutic treatment of erectile dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 35 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:905783 CAPLUS
DN 137:389159
TI Delivery of erectile dysfunction drugs through an inhalation route
IN Rabinowitz, Joshua D.; Zaffaroni, Alejandro C.
PA Alexza Molecular Delivery Corporation, USA
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 21

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002094219	A2	20021128	WO 2002-US16398	20020522
	WO 2002094219	A3	20030306		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003017115	A1	20030123	US 2002-146516	20020513
	WO 2003026631	A1	20030403	WO 2002-US18543	20020513
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003007933	A1	20030109	US 2002-150267	20020515
	US 2003007934	A1	20030109	US 2002-150268	20020515
	US 2003017117	A1	20030123	US 2002-151596	20020516
	US 2003206869	A1	20031106	US 2002-151626	20020516
	US 2003017116	A1	20030123	US 2002-150857	20020517
	US 2003021753	A1	20030130	US 2002-150591	20020517
	US 2003005924	A1	20030109	US 2002-152652	20020520
	US 2003012740	A1	20030116	US 2002-153139	20020520
	US 2003017118	A1	20030123	US 2002-152639	20020520
	US 2003021754	A1	20030130	US 2002-152640	20020520
	US 2003012737	A1	20030116	US 2002-153311	20020521
	US 2003015189	A1	20030123	US 2002-153831	20020521
	US 2003017119	A1	20030123	US 2002-153839	20020521
	US 2003017120	A1	20030123	US 2002-155703	20020522
	US 2003021755	A1	20030130	US 2002-155705	20020522
	US 2003000518	A1	20030102	US 2002-155097	20020523
	US 2003015190	A1	20030123	US 2002-154594	20020523
	US 2003017114	A1	20030123	US 2002-154765	20020523
PRAI	US 2001-294203P	P	20010524		
	US 2001-317479P	P	20010905		

AB The present invention relates to aerosols contg. erectile dysfunction drugs that are used in inhalation therapy. The aerosol comprises particles comprising at least 5% by wt. of an erectile dysfunction drug.

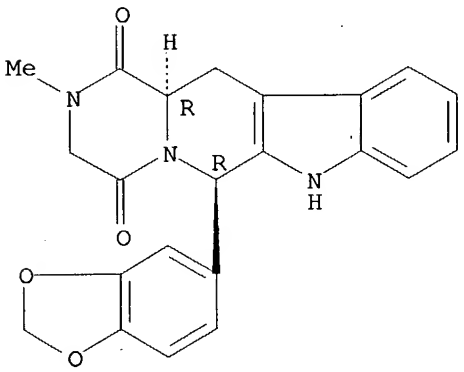
The method comprises: a) heating a compn., wherein the compn. comprises at least 5% by wt. of an erectile dysfunction drug, to form a vapor; and, b) allowing the vapor to cool, thereby forming a condensation aerosol comprising particles, which is inhaled by the mammal. Kits are described and a general procedure for volatilizing compds. is given.

IT **171596-29-5**, Tadalafil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delivery of erectile dysfunction drugs through an inhalation route)

RN 171596-29-5 CAPLUS

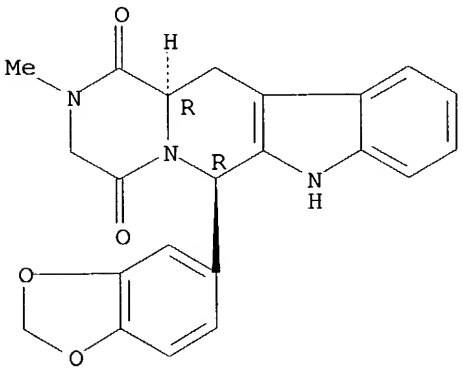
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 36 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:899323 CAPLUS
DN 139:78085
TI Phosphodiesterase 5 inhibitors
AU Stamford, Andrew W.
CS Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SO Annual Reports in Medicinal Chemistry (2002), 37, 53-64
CODEN: ARMCBI; ISSN: 0065-7743
PB Elsevier Science
DT Journal; General Review
LA English
AB A review discusses the clin. development of phosphodiesterase5 inhibitors for the treatment of erectile dysfunction (ED), and the recent advances in the medicinal chem. of selective PDE5 inhibitors that have been reported. It also discusses the potential therapeutic indications for PDE5 inhibitors other than for ED.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 5 inhibitors for treating impotence)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

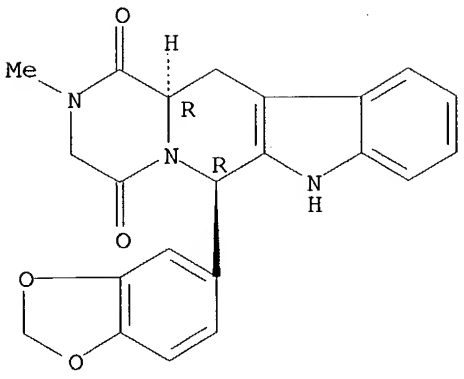
Absolute stereochemistry. Rotation (+).



RE.CNT 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 37 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:875588 CAPLUS
DN 138:378373
TI Selective phosphodiesterase type 5 inhibition using tadalafil for the treatment of erectile dysfunction
AU Kuan, James; Brock, Gerald
CS Dept. of Surgery, Division of Urology, St. Joseph's Health Centre, London, ON, Can.
SO Expert Opinion on Investigational Drugs (2002), 11(11), 1605-1613
CODEN: EOIDER; ISSN: 1354-3784
PB Ashley Publications Ltd.
DT Journal; General Review
LA English
AB A review. Erectile dysfunction (ED) pharmacotherapy has undergone dramatic advances over the past decade, since the introduction of phosphodiesterase type 5 inhibitors (PDE5). The availability of an oral agent, sildenafil, able to restore erectile function in the majority of men with an org. basis to their dysfunction, transformed the management. The nos. of men seeking medical attention for ED, along with the increased comfort of physicians treating it, has resulted in enhanced management of this condition. In spite of these advances, there exist a significant no. of men who remain unsuccessfully treated with sildenafil. Development of new PDE5 inhibitors, with the promise of enhanced selectivity, longer duration of action, increased potency and greater ease of use are currently in the final stages of regulatory review in many countries. Tadalafil is the first such agent to gain preliminary EU approval and is reviewed in detail in this report. Focusing on its phase II/III trial results, tadalafil appears to have an enhanced period of responsiveness extending out to 36 h in 60% of men using the 20 mg dose. Efficacy across a large population of men with ED of various causes (n = 1112) is in accordance with the other PDE5 inhibitors at 81%. Side effects are generally mild-to-moderate with study drop-out rate at 1.7% in the active arm compared to 1.1% among those receiving placebo. In summary, this agent will likely play an important role in the management of ED across a broad spectrum of etiologies, once past the ongoing regulatory review process.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective PDE5 inhibition using tadalafil for treatment of erectile dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

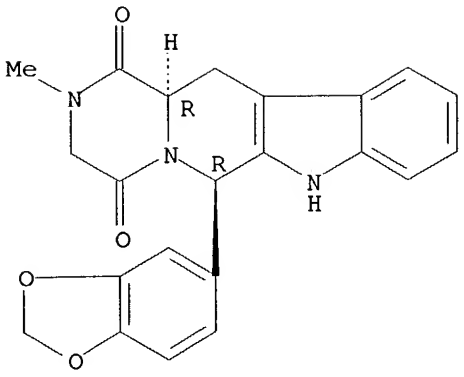
Absolute stereochemistry. Rotation (+).



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 38 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:820932 CAPLUS
DN 137:304567
TI Efficacy and safety of tadalafil for the treatment of erectile dysfunction: results of integrated analyses
AU Brock, Gerald B.; McMahon, Chris G.; Chen, K. K.; Costigan, Timothy; Shen, Wei; Watkins, Vish; Anglin, Greg; Whitaker, Steve
CS Department of Surgery, Division of Urology, Faculty of Medicine and Dentistry, University of Western Ontario, London, ON, Can.
SO Journal of Urology (Hagerstown, MD, United States) (2002), 168(4, Pt. 1), 1332-1336
CODEN: JOURAA; ISSN: 0022-5347
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB We conducted integrated analyses of the efficacy and safety of tadalafil, a potent, selective phosphodiesterase 5 inhibitor, for the treatment of erectile dysfunction. A total of 1,112 men with a mean age of 59 yr (range 22 to 82) and mild to severe erectile dysfunction of various etiologies were randomized to placebo or tadalafil, taken as needed without food or alc. restrictions, at fixed daily doses of 2.5 mg., 5 mg., 10 mg., or 20 mg. in 5 randomized, double-blind, placebo controlled trials lasting 12 wk. The 3 co-primary outcomes were changes from baseline in the erectile function domain of the International Index of Erectile Function and the proportion of "yes" responses to questions 2 and 3 of the Sexual Encounter Profile. Addnl. efficacy instruments included a Global Assessment Question. Compared with placebo, tadalafil significantly enhanced all efficacy outcomes. Patients receiving 20 mg. tadalafil experienced a significant mean improvement of 7.9 in International Index of Erectile Function erectile function domain score from baseline ($p < 0.001$ vs. placebo), 75% of intercourse attempts (Sexual Encounter Profile question 3, a secondary efficacy outcome) were successfully completed ($p < 0.001$ vs. placebo) and 81% reported improved erections at end point compared with 35% in the control group ($p < 0.001$). Tadalafil was consistently efficacious across disease severities and etiologies, as well as in patients of all ages. Tadalafil was well tolerated, and headache and dyspepsia were the most frequent adverse events. Tadalafil was effective and well tolerated in this patient population.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tadalafil for treatment of erectile dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

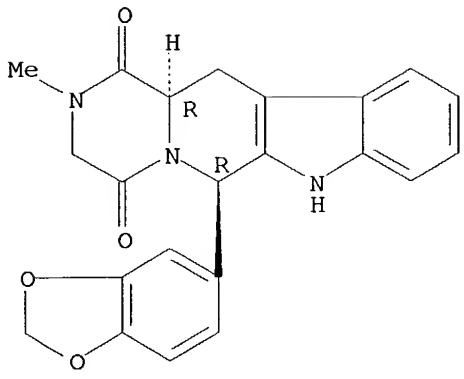
L5 ANSWER 39 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:792003 CAPLUS
DN 137:299922
TI Nasal spray compositions containing cGMP-PDE inhibitors and local anesthetics for the treatment of male erectile disfunction
IN Serno, Peter; Ohm, Andreas; Barth, Wolfgang; Bauer, Richard-Josef; Siefert, Hans-Martin; Zimmer, Dieter
PA Bayer AG, Germany
SO Ger. Offen., 12 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10118305	A1	20021017	DE 2001-10118305	20010412
	WO 2002083108	A2	20021024	WO 2002-EP3977	20020410
	WO 2002083108	A3	20030410		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI DE 2001-10118305 A 20010412
OS MARPAT 137:299922
AB The present invention concerns compns. for nasal application of cGMP-PDE inhibitors, in particular of PDE5-inhibitors, and local anesthetics; local anesthetics is not benzylalc. The compns. further contain antioxidants, surfactants, stabilizers, wetting agents, etc.; nasal sprays and powder inhalants are claimed. Thus a powder compn. contained (kg): Sildenafil citrate, micronized 25.0; lidocaine hydrochloride 10.0; lactose 65.0. The homogenized mixt. was filled in aliquots of 20 mg into inhaler vials.
IT **171596-29-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nasal compns. contg. cGMP-PDE inhibitors and local anesthetics for treatment of male erectile disfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).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L5 ANSWER 40 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:777881 CAPLUS
DN 137:278918
TI Preparation of cyclopentyl-substituted glutaric acid monoamides as neutral endopeptidase inhibitors for treating female sexual arousal disorder and related conditions
IN Challenger, Stephen; Cook, Andrew Simon; Gillmore, Adam Thomas; Middleton, Donald Stuart; Pryde, David Cameron; Stobie, Alan
PA Pfizer Limited, UK; Pfizer Inc.
SO PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002079143	A1	20021010	WO 2002-IB807	20020318
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003105132	A1	20030605	US 2002-96218	20020312
	US 6660756	B2	20031209		
PRAI	GB 2001-7750	A	20010328		
	GB 2001-13112	A	20010530		
	GB 2001-20152	A	20010817		
	US 2001-292485P	P	20010521		
	US 2001-299031P	P	20010618		
	US 2001-317777P	P	20010906		

OS MARPAT 137:278918
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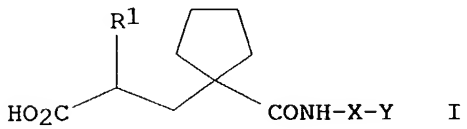

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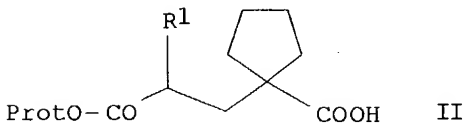


II

AB The invention relates to cyclopentyl-substituted glutaric acid monoamides (shown as I; e.g. (2S)-2-[[1-[[[3-(4-chlorophenyl)propyl]amino]carbonyl]cyclopentyl]methyl]-4-methoxybutanoic acid), inhibition of neutral endopeptidase (NEP) enzyme, methods of prepn. and uses, e.g. treating

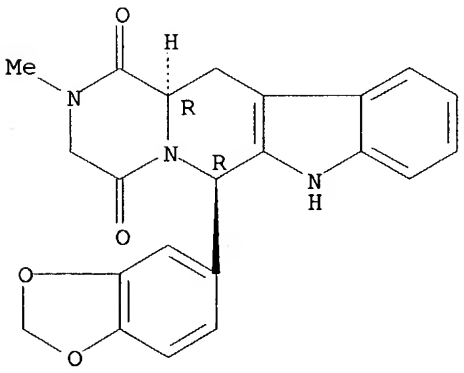
female sexual arousal disorder. In I, R1 is optionally substituted C1-6alkyl, carbocyclyl, heterocyclyl, H, C1-6alkoxy, amino, or sulfonylamino. X is the linkage -(CH2)n- or -(CH2)q-O- (wherein Y is attached to the O); wherein one or more H atoms in linkage X may be replaced independently by C1-4alkoxy; hydroxy; hydroxyC1-3alkyl; C3-7cycloalkyl; carbocyclyl; heterocyclyl; or by C1-4alkyl optionally substituted by one or more fluoro or Ph groups; n is 3-7; and q is 2-6; and Y is optionally substituted Ph or pyridyl. One process for prepg. I involves reacting II (Prot = protecting group) with Y-X-NH2 to give protected I, which is then deprotected and later optionally converted to a salt; other methods involve asym. hydrogenation of an alkene precursor to II. More than 100 example prepns. of intermediates and claimed compds. are included; most of the claimed compds. are N-phenpropyl amides. IC50 values against neutral endopeptidase and selectivity against neutral endopeptidase vs. ACE are given for some of the claimed compds.; for example, 3-[1-[[[3-(2,3-dihydrobenzofuran-5-yl)propyl]amino]carbonyl]cyclopentyl]propanoic acid showed an IC50 against NEP of 3 nM and a >300 selectivity against ACE. Test results for use of (2S)-2-[[1-[[[3-(4-chlorophenyl)propyl]amino]carbonyl]cyclopentyl]methyl]-4-methoxybutanoic acid in rabbit models of female sexual arousal response and male erectile response are included.

IT **171596-29-5**, (6R,12AR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination with cyclopentyl-substituted glutaric acid monoamide neutral endopeptidase inhibitors for treating female sexual arousal disorder and related conditions)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

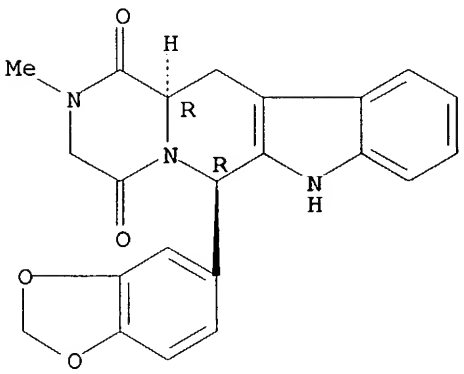
Absolute stereochemistry. Rotation (+).



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 41 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:551103 CAPLUS
DN 137:103318
TI Tadalafil: an oral selective phosphodiesterase 5 inhibitor for treatment of erectile dysfunction
AU Kim, Sunghyun; Narayanan, Seethalakshmi; Song, Jessica C.
CS Department of Pharmacy Services, St Joseph's Medical Center, Stockton, CA, USA
SO Formulary (2002), 37(6), 289-290, 293-296
CODEN: FORMF9; ISSN: 1082-801X
PB Advanstar Communications, Inc.
DT Journal; General Review
LA English
AB A review. Tadalafil (IC351) is a selective inhibitor of phosphodiesterase 5 (PDE5) under FDA review for treatment of erectile dysfunction (ED) and diabetes-related ED. If approved, it will join the widely used PDE5 inhibitor sildenafil citrate as an oral therapy for ED management. Placebo-controlled trials have shown tadalafil to be safe and effective at doses of 5 to 25 mg for treating ED and doses of 10 to 20 mg for treating diabetes-related ED. Tadalafil is rapidly absorbed, and patients have shown responsiveness (with multiple successful intercourse attempts) for up to 24 h after administration. Tadalafil undergoes hepatic metab. and is largely metabolized by the cytochrome P 450 3A4 isoenzyme. Headache and dyspepsia have been the most common adverse effects reported with the drug. According to the results from the largest clin. trials conducted to date, tadalafil has produced no abnormal visual effects and no clin. significant changes in blood pressure or electrocardiog. parameters.
IT **171596-29-5**, Tadalafil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tadalafil, oral selective phosphodiesterase 5 inhibitor for treatment of erectile dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

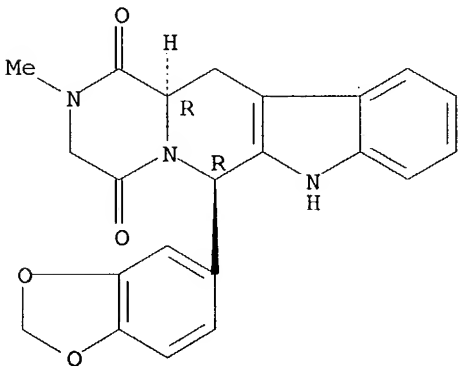
Absolute stereochemistry. Rotation (+).



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 42 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:524539 CAPLUS
DN 137:87748
TI Tadalafil (Cialis) for men with erectile dysfunction
AU Eardley, I.; Cartledge, J.
CS Department of Urology, St James' University Hospital, Leeds, UK
SO International Journal of Clinical Practice (2002), 56(4), 300-304
CODEN: IJCPF9; ISSN: 1368-5031
PB Medicom International
DT Journal; General Review
LA English
AB A review. Tadalafil is an inhibitor of phosphodiesterase type 5, and is currently undergoing regulatory review in the US and in Europe. Its chem. structure is significantly different from sildenafil, and in vitro studies confirm significant potency for PDE5 inhibition, with little activity against most of the other isoforms of the enzyme including PDE6, which is the isoform of the enzyme found within the retina. The half-life of tadalafil is 17.5 h and clin. studies suggest significant activity 24 h post-dosing. As with sildenafil, efficacy depends upon a normal sexual stimulus, and the drug can taken be as required. Tadalafil is effective in the treatment of men with erectile dysfunction, and it appears to have a relatively mild side-effect profile, with no visual side-effects noted.
IT **171596-29-5**, Cialis
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tadalafil (Cialis) for men with erectile dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

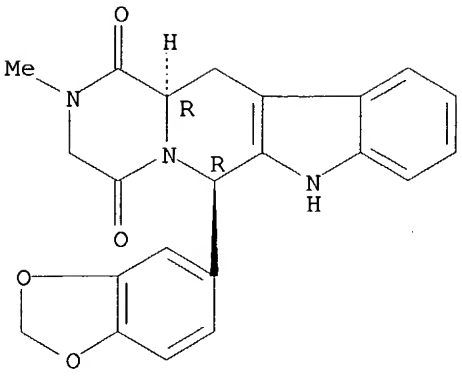
L5 ANSWER 43 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:427673 CAPLUS
DN 137:3711
TI Cells and animals homozygous or heterozygous for a knockout of the PDE11A gene and their uses
IN Burslem, Martin F.; Harrow, Ian Dennis; Lanfear, Jeremy; Phillips, Stephen C.
PA Pfizer Limited, UK; Pfizer Inc.
SO Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1211313	A2	20020605	EP 2001-308959	20011022
	EP 1211313	A3	20030423		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003061625	A1	20030327	US 2001-40570	20011101
PRAI	GB 2000-26727	A	20001101		
	GB 2001-11710	A	20010514		
	US 2000-255689P	P	20001214		
	US 2001-293411P	P	20010524		

AB Animal cells and animals carrying a knockout of the gene for the cyclic nucleotide phosphodiesterase PDE11 are described for use in anal. of the role of the enzyme, esp. in spermatogenesis and in the screening of drugs for regulation of spermatogenesis. Heterozygous knockout mice show lowered levels of spermatogenesis. The effect of the knockout on patterns of gene expression was analyzed by microarray hybridization. Known inhibitors of cyclic nucleotide phosphodiesterases were tested for their ability to inhibit PDE11. The pattern of inhibition was similar to, but distinct from, that for PDE5. Array hybridization was used to analyze the effects of PDE11 knockout on gene expression in testis. Twenty-four genes (18 down-regulated and 6 up-regulated) were identified. These gene products may themselves be therapeutic targets for PDE11-related disease (no data).

IT **171596-29-5**, IC-351
RL: PAC (Pharmacological activity); BIOL (Biological study)
(as inhibitor of PDE11; cells and animals homozygous or heterozygous for knockout of PDE11A gene and their uses)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).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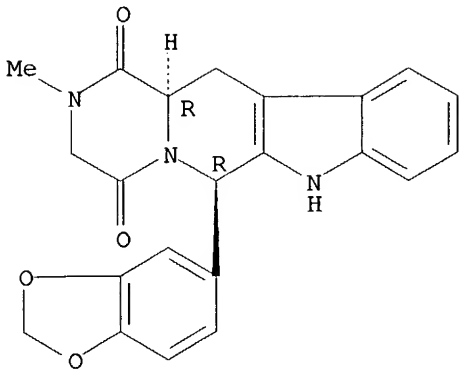
L5 ANSWER 44 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:391540 CAPLUS
DN 136:380144
TI Phosphodiesterase V inhibitors for the treatment of premature ejaculation
IN Boolell, Mitradev
PA Pfizer Limited, UK; Pfizer Inc.
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002040027	A1	20020523	WO 2001-IB2180	20011119
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002091129	A1	20020711	US 2001-990955	20011116
	AU 2002015149	A5	20020527	AU 2002-15149	20011119
	EP 1335730	A1	20030820	EP 2001-983728	20011119
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001015413	A	20031007	BR 2001-15413	20011119
PRAI	GB 2000-28245	A	20001120		
	US 2001-260564P	P	20010109		
	WO 2001-IB2180	W	20011119		

AB The invention relates to the use of cGMP phosphodiesterase V inhibitors, including in particular the compd. sildenafil, for the treatment of premature ejaculation in patients with normal erectile function.
IT **171596-29-5**, IC 351
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase V inhibitors for treatment of premature ejaculation)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

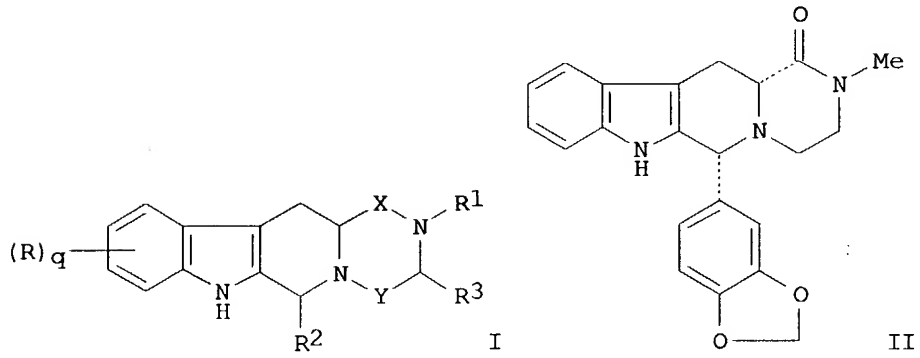


RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 45 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:353456 CAPLUS
DN 136:369739
TI Preparation of pyrazino[1',2':1,6]pyrido[3,4-b]indole derivatives as phosphoesterase inhibitors for use as therapeutic agents
IN Orme, Mark W.; Sawyer, Jason Scott; Schultze, Lisa M.
PA Lilly Icos L.L.C., USA
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002036593	A1	20020510	WO 2001-US31364	20011009
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002011493	A5	20020515	AU 2002-11493	20011009
	EP 1332144	A1	20030806	EP 2001-979546	20011009
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003229080	A1	20031211	US 2003-398720	20030409
PRAI	US 2000-246257P	P	20001106		
	WO 2001-US31364	W	20011009		

OS MARPAT 136:369739
GI



I II

AB 2,3,6,7,12,12A-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indole derivs., such as I [R = halo, alkyl; R1 = H, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, heteroarylalkyl, etc.; R2 = monocyclic arom. ring, such as benzene, thiophene, furan, pyridine, etc.; R3 = H, alkyl; R1,R3 = fused carbocyclic ring; X, Y = CO, SO, SO2, CS, C(Ra)2; Ra = H, alkyl, benzyl; q

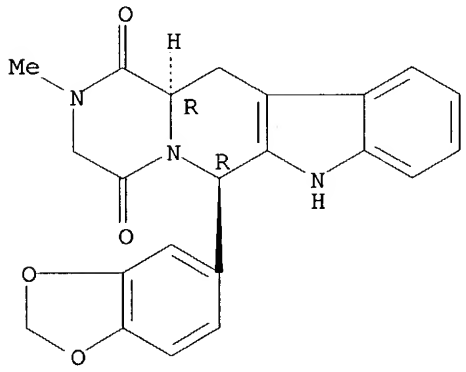
= 0-4], pharmaceutically acceptable salts and solvates thereof, were prepd. for pharmaceutical use as phosphodiesterase inhibitors for the treatment of conditions such as erectile dysfunction, female arousal disorder, angina, hypertension, and vascular disease. Thus, pyrazinopyridoindole deriv. II was prepd. by a multistep procedure starting with D-tryptophan Me ester, piperonal and chloroacetaldehyde. The prepd. heterocycles were tested for phosphodiesterase V (PDE5) inhibitory activity with II exhibiting an IC50 of 54 nM.

IT **171596-29-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of pyrazino[1',2':1,6]pyrido[3,4-b]indole derivs. as phosphoesterase inhibitors for use as therapeutic agents)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 46 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:314395 CAPLUS
DN 136:335540
TI Use of PDE V inhibitors for improved fecundity in mammals
IN Westbrook, Simon Lempriere; Zanzinger, Johannes Friedrich
PA Pfizer Limited, UK; Pfizer Inc.
SO Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

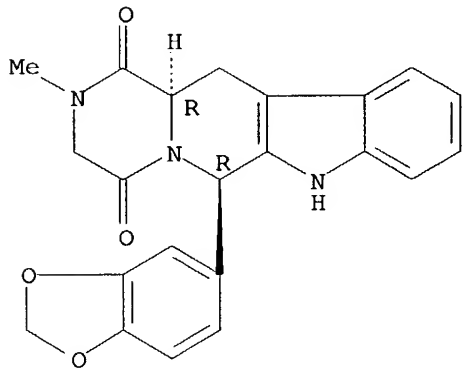
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1199070	A2	20020424	EP 2001-308684	20011011
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003018036	A1	20030123	US 2001-982445	20011018
	US 6548508	B2	20030415		
	JP 2002220346	A2	20020809	JP 2001-322195	20011019
	US 2003018037	A1	20030123	US 2002-229534	20020827
PRAI	GB 2000-25782	A	20001020		
	US 2000-253338P	P	20001128		
	US 2001-982445	A1	20011018		

AB The invention relates to the use of a cyclic guanosine 3',5'-monophosphate phosphodiesterase type five (cGMP PDE V) inhibitor for increasing fecundity in a mammal by one or more of (a) promoting the growth of an oocyte, zygote, blastocyst, embryo and/or fetus, (b) increasing the rate or probability of survival of an embryo and/or fetus and (c) increasing the birth wt. of a progeny, or for increasing milk productivity. I.v. and tablet formulations are exemplified. Formulations and packs contg. the PDE V inhibitors for pharmaceutical or veterinary use are claimed.

IT **171596-29-5**, IC-351
RL: AGR (Agricultural use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of PDE V inhibitors for improved fecundity in mammals)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 47 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:241329 CAPLUS
DN 136:284433
TI Administration of phosphodiesterase inhibitors for the treatment of premature ejaculation
IN Wilson, Leland F.; Doherty, Paul C.; Place, Virgil A.; Smith, William L.; Abdel-Hamid, Abdou Ali Ibrahim Aboubakr
PA USA
SO U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 467,094.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 7

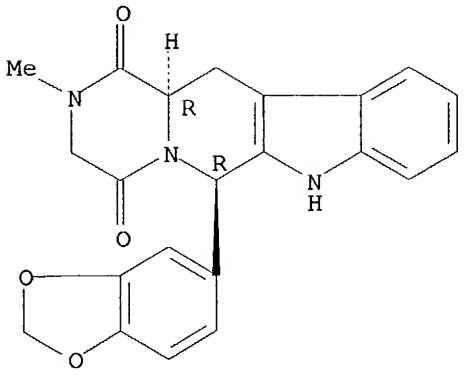
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002037828	A1	20020328	US 2001-888250	20010621
	US 6403597	B2	20020611		
	US 6037346	A	20000314	US 1998-181070	19981027
	US 6548490	B1	20030415	US 1999-467094	19991210
	WO 2003000343	A2	20030103	WO 2002-US9415	20020325

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 1997-958816 B2 19971028
US 1998-181070 A2 19981027
US 1999-467094 A2 19991210
US 2001-888250 A 20010621

AB A method is provided for treatment of premature ejaculation by administration of a phosphodiesterase inhibitor, e.g., an inhibitor of a Type III, Type IV, or Type V phosphodiesterase. In a preferred embodiment, administration is on as "as needed" basis, i.e., the drug is administered immediately or several hours prior to sexual activity. Pharmaceutical formulations and packaged kits are also provided. Zaprinast 1.0, mannitol 1.0, microcryst. cellulose 2.0, and magnesium stearate 10 mg are blended in a suitable mixer and then compressed into sublingual tablets. Each sublingual tablet contains 10 mg zaprinast.
IT **171596-29-5**, GF 196960
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GF 196960; administration of phosphodiesterase inhibitors for treatment of premature ejaculation)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).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L5 ANSWER 48 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:142493 CAPLUS
DN 136:194255
TI Treatment of the insulin resistance syndrome
IN Fryburg, David Albert; Gibbs, Earl Michael; Koppiker, Nandan Parmanand
PA Pfizer Limited, UK; Pfizer Inc.
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002013798	A2	20020221	WO 2001-IB1428	20010806
	WO 2002013798	A3	20030123		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001076607	A5	20020225	AU 2001-76607	20010806
	EP 1307183	A2	20030507	EP 2001-954266	20010806
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2002165237	A1	20021107	US 2001-927525	20010810
	WO 2002060422	A2	20020808	WO 2002-IB315	20020130
	WO 2002060422	A3	20021010		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002143015	A1	20021003	US 2002-60788	20020130
	EP 1355651	A2	20031029	EP 2002-716245	20020130
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003166662	A1	20030904	US 2003-368826	20030219
PRAI	US 2000-224928P	P	20000811		
	GB 2000-30649	A	20001215		
	US 2001-266083P	P	20010202		
	GB 2001-6465	A	20010315		
	GB 2001-6468	A	20010315		
	GB 2001-17134	A	20010713		
	US 2000-256431P	P	20001218		
	US 2001-292506P	P	20010521		
	WO 2001-IB1428	W	20010806		
	US 2001-927525	B1	20010810		
	WO 2002-IB315	W	20020130		

AB Use of a selective cGMP PDE5 inhibitor or a pharmaceutical compn. thereof

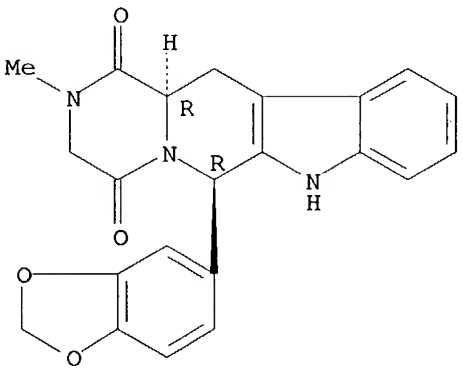
in the prepn. of a medicament for the curative, palliative or prophylactic treatment of the insulin resistance syndrome wherein the insulin resistance syndrome means the concomitant existence in a subject of two or more of: dyslipidemia; hypertension; type 2 diabetes mellitus, impaired glucose tolerance (IGT) or a family history of diabetes; hyperuricemia and/or gout; a pro-coagulant state; atherosclerosis; or truncal obesity wherein said use can occur alone or in combination with other agents to treat the insulin resistance syndrome or individual aspects of the insulin resistance syndrome.

IT **171596-29-5,** IC-351
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of insulin resistance syndrome)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

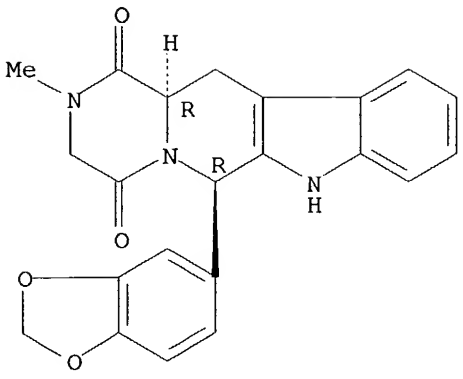


L5 ANSWER 49 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:122770 CAPLUS
DN 136:178015
TI Drugs for incontinence - salified and nonsalified nitric oxide-donors and phosphodiesterase inhibitors
IN Del Soldato, Piero; Benedini, Francesca
PA Nicox S.A., Fr.
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002011707	A2	20020214	WO 2001-EP8734	20010727
	WO 2002011707	A3	20021205		
	W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001091691	A5	20020218	AU 2001-91691	20010727
	EP 1307184	A2	20030507	EP 2001-971798	20010727
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003203899	A1	20031030	US 2003-343330	20030206
PRAI	IT 2000-MI1848	A	20000808		
	WO 2001-EP8734	W	20010727		

OS MARPAT 136:178015
AB Use in the incontinence of one or more of the following classes of drugs selected from the following: (B) salified and nonsalified nitric oxide-donor drugs, of formula: A - X1 - N(O)z, (B') nitrate salts of drugs used for the incontinence, and which do not contain in the mol. a nitric oxide donor group; (C) org. or inorg. salts of compds. inhibiting phosphodiesterases.
IT **171596-29-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salified and nonsalified nitric oxide-donors and phosphodiesterase inhibitors for treatment of incontinence)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).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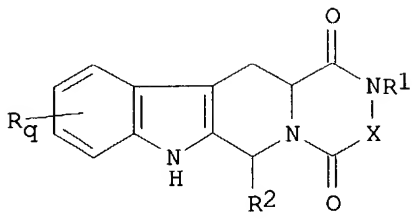
L5 ANSWER 50 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:107344 CAPLUS
DN 136:151441
TI Preparation of fused heterocyclic derivatives as phosphodiesterase inhibitors
IN Orme, Mark W.; Sawyer, Jason Scott; Schultze, Lisa M.
PA Lilly Icos L.L.C., USA
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002010166	A1	20020207	WO 2001-US21678	20010709
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001071948	A5	20020213	AU 2001-71948	20010709
	EP 1305313	A1	20030502	EP 2001-951008	20010709
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003207867	A1	20031106	US 2003-333146	20030115
PRAI	US 2000-222451P	P	20000802		
	WO 2001-US21678	W	20010709		

OS MARPAT 136:151441
GI



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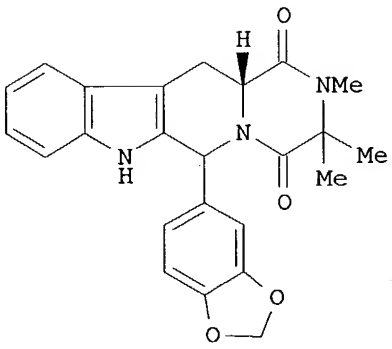


II

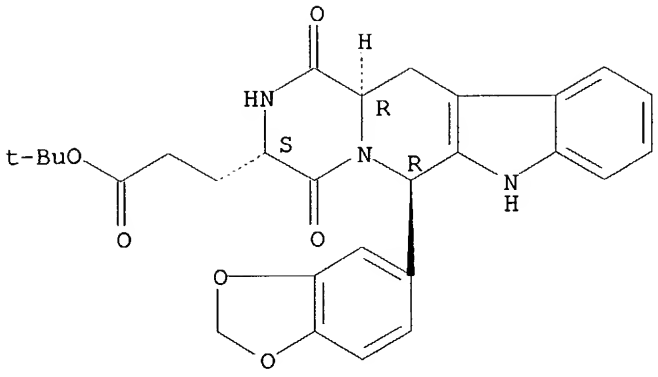
AB Compds. I [R = halo, alkyl; q = 0-4; R1 = H, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, cycloalkylalkyl, arylalkyl, heteroarylalkyl; R2 is an optionally substituted monocyclic arom. ring selected from benzene, thiophene, furan, and pyridine or an optionally substituted bicyclic ring; X = NH or substituted imino, O, S, substituted methylene or ethylene; the substituents may form addnl. rings] and their salts and solvates were prepd. for use as phosphodiesterase (PDE) inhibitors. Thus, compd. II was prepd. by a multistep procedure starting with coupling of L-tryptophan Me ester with CbzNMeCMe2CO2H (Cbz = benzyloxycarbonyl) and showed IC50 = 161.0 nM for inhibition of cGMP-PDE.

IT **395665-39-1P 395665-40-4P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of fused heterocyclic derivs. as phosphodiesterase inhibitors)

RN 395665-39-1 CAPLUS

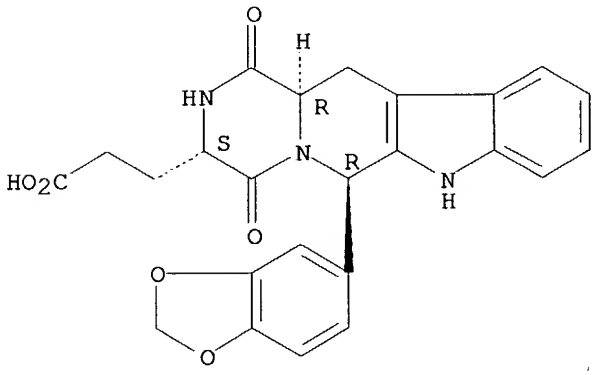
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-propanoic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, 1,1-dimethylethyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 395665-40-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-propanoic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

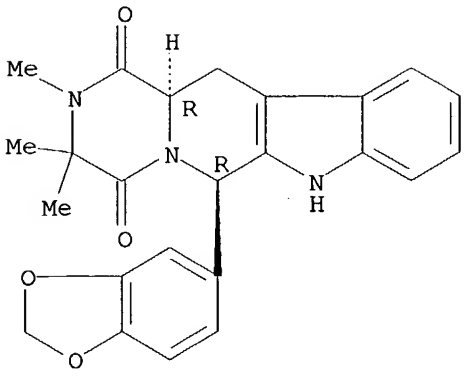
Absolute stereochemistry. Rotation (+).



IT **395665-35-7P 395665-36-8P 395665-41-5P**
395665-42-6P 395665-47-1P 395665-49-3P
395665-51-7P 395665-53-9P 395665-55-1P
395665-57-3P 395665-59-5P 395665-61-9P
395665-63-1P 395665-65-3P 395665-67-5P
395665-69-7P 395665-70-0P 395665-71-1P
395665-72-2P 395665-73-3P 395665-75-5P
395665-76-6P 395665-77-7P 395665-78-8P
395665-79-9P 395665-80-2P 395665-81-3P
395665-91-5P 395665-95-9P 395665-96-0P
395665-98-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of fused heterocyclic derivs. as phosphodiesterase inhibitors)

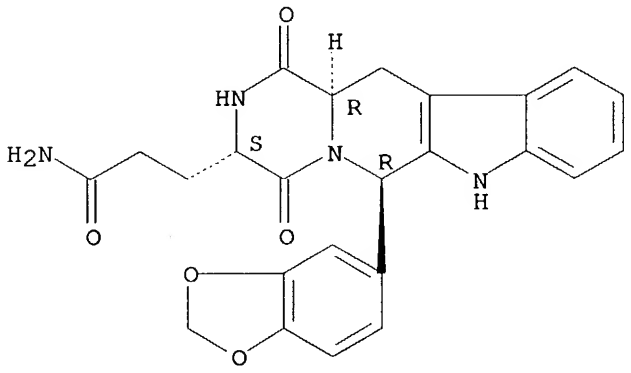
RN 395665-35-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3,3-trimethyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



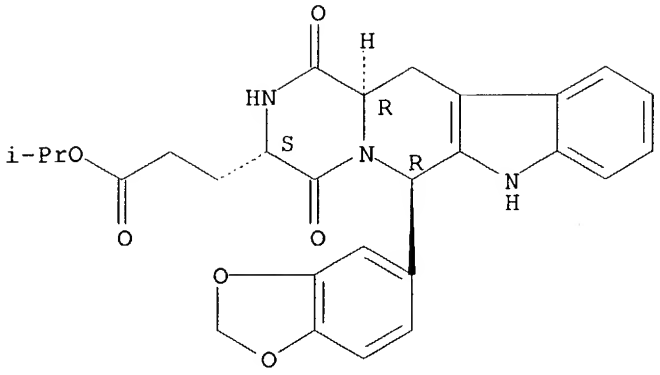
RN 395665-36-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-propanamide, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



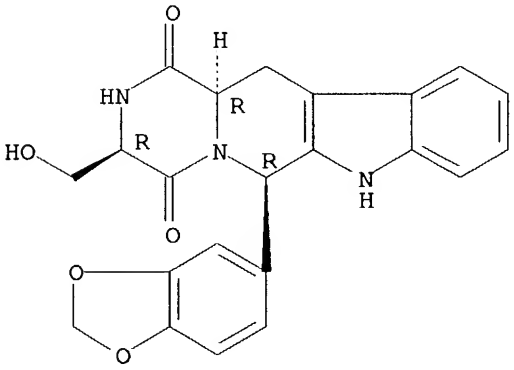
RN 395665-41-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-propanoic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, 1-methylethyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



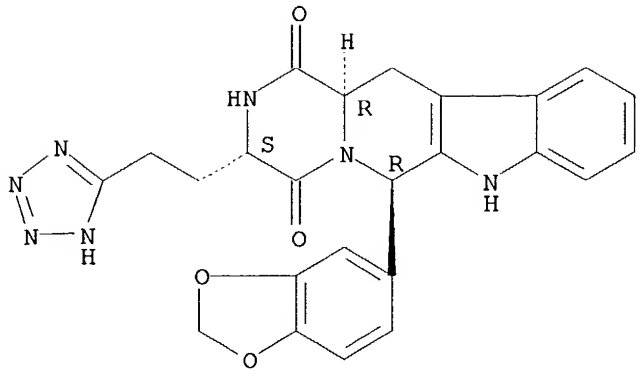
RN 395665-42-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-(hydroxymethyl)-, (3R,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



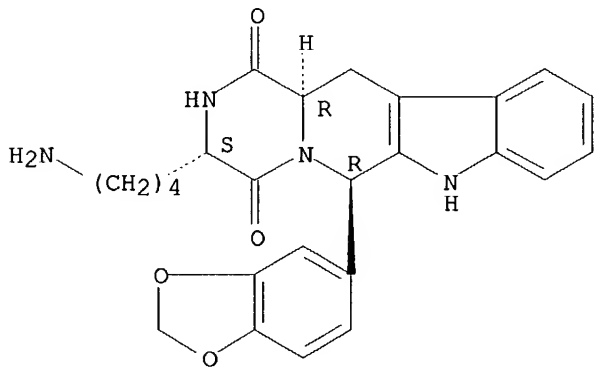
RN 395665-47-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-[2-(1H-tetrazol-5-yl)ethyl]-, (3S,6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



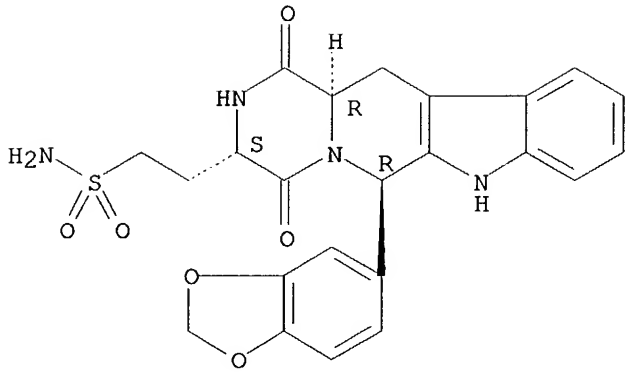
RN 395665-49-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 3-(4-aminobutyl)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



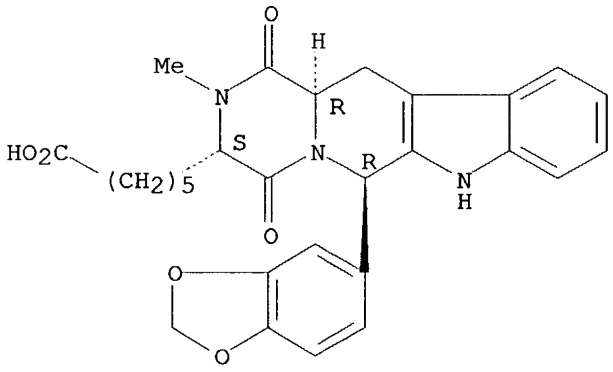
RN 395665-51-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-ethanesulfonamide, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



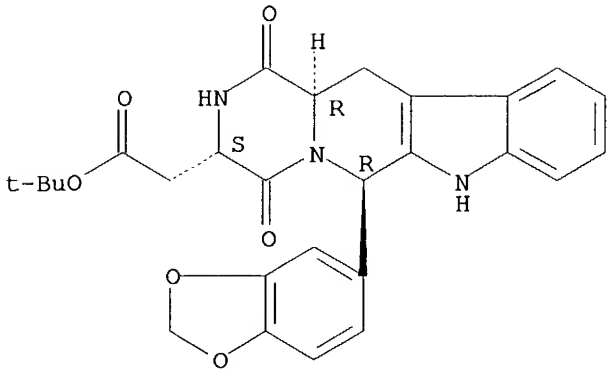
RN 395665-53-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-hexanoic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxo-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



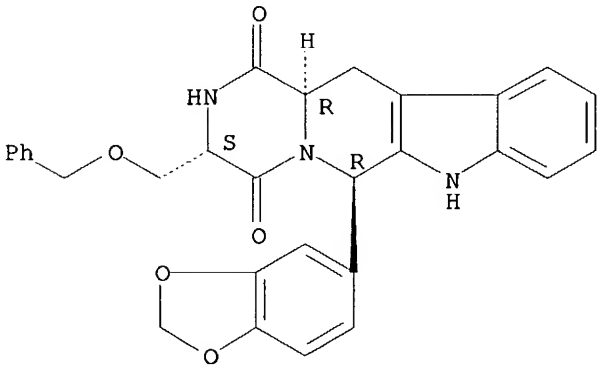
RN 395665-55-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, 1,1-dimethylethyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



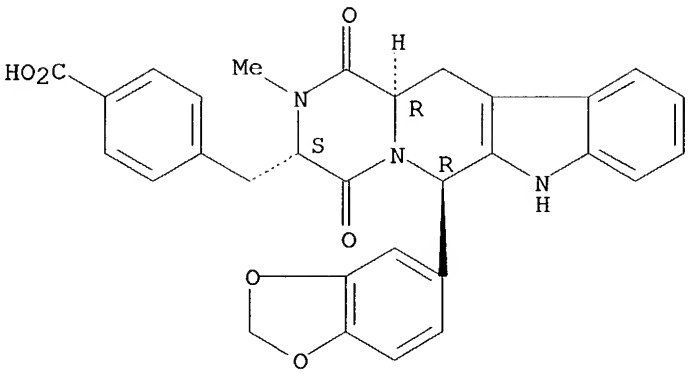
RN 395665-57-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-[(phenylmethoxy)methyl]-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



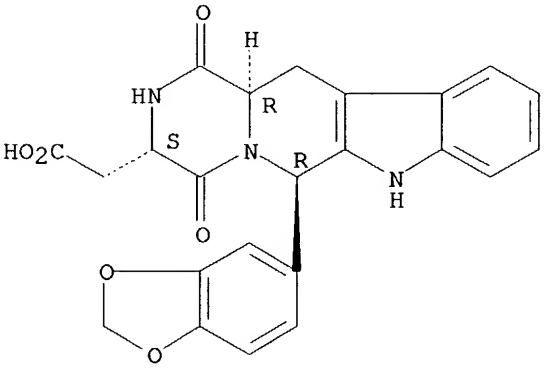
RN 395665-59-5 CAPLUS
CN Benzoic acid, 4-[[(3S,6R,12aR)-6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



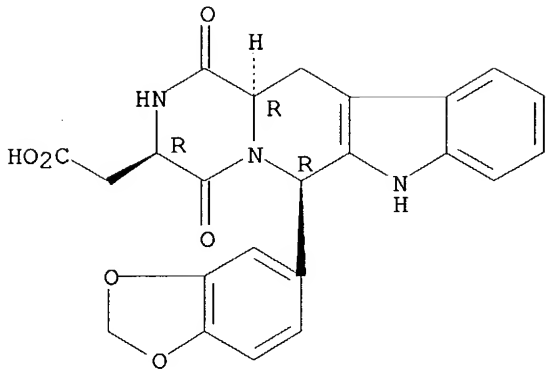
RN 395665-61-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



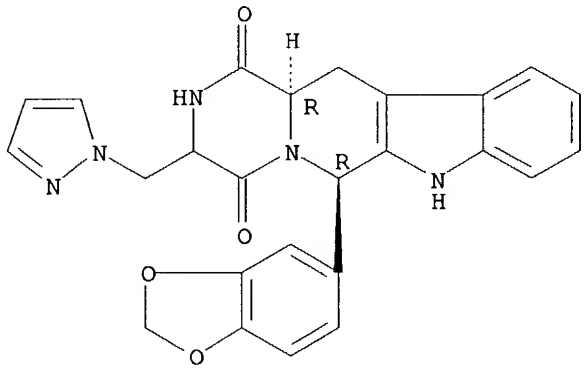
RN 395665-63-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, (3R,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



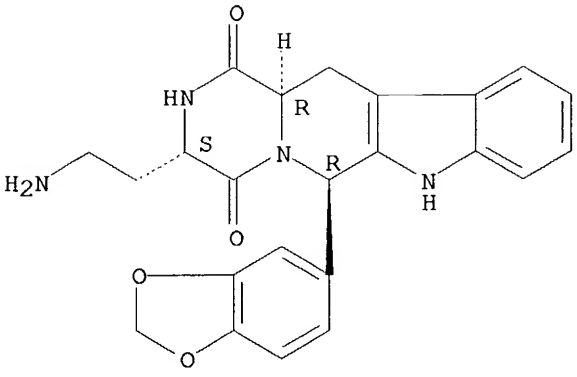
RN 395665-65-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-(1H-pyrazol-1-ylmethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



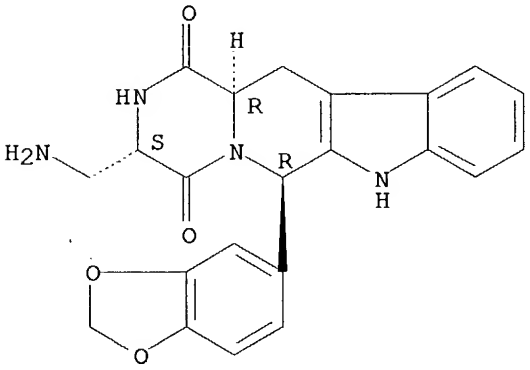
RN 395665-67-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 3-(2-aminoethyl)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



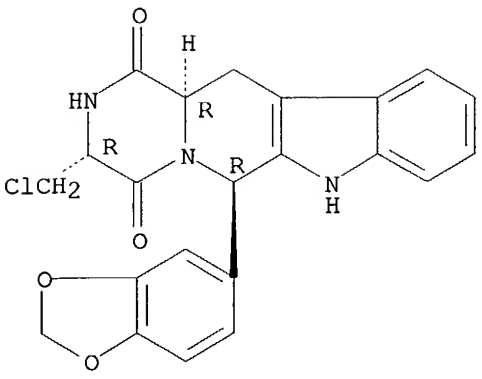
RN 395665-69-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 3-(aminomethyl)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



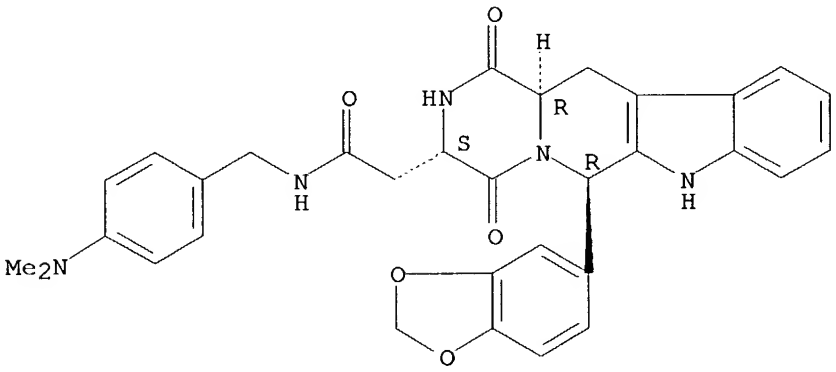
RN 395665-70-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-3-(chloromethyl)-2,3,6,7,12,12a-hexahydro-, (3R,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



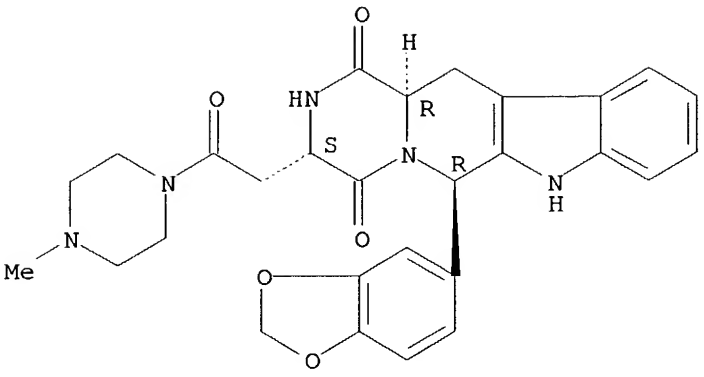
RN 395665-71-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetamide, 6-(1,3-benzodioxol-5-yl)-N-[[4-(dimethylamino)phenyl]methyl]-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



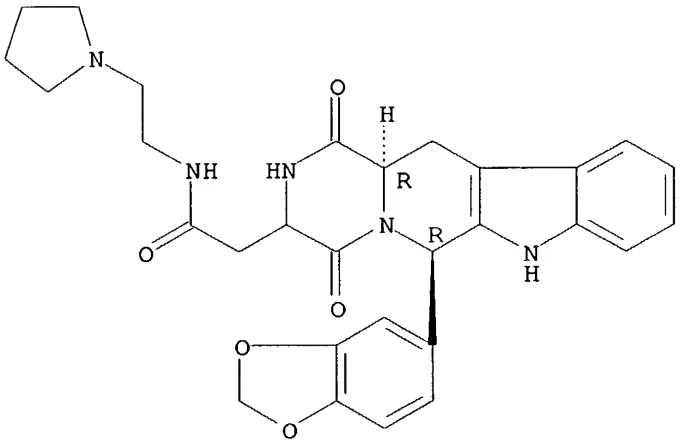
RN 395665-72-2 CAPLUS
CN Piperazine, 1-[[(3S,6R,12aR)-6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-3-yl]acetyl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



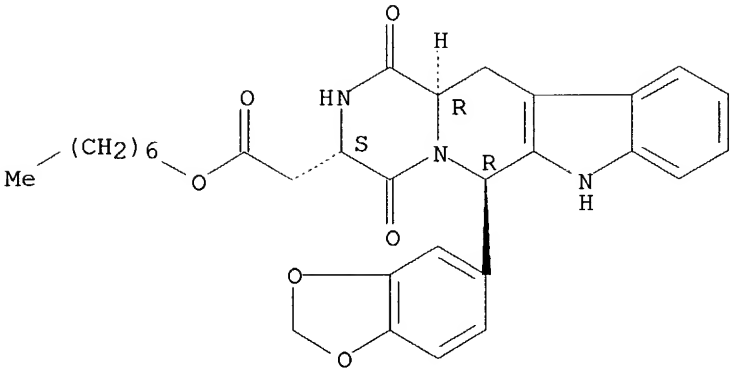
RN 395665-73-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetamide, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-N-[2-(1-pyrrolidinyl)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



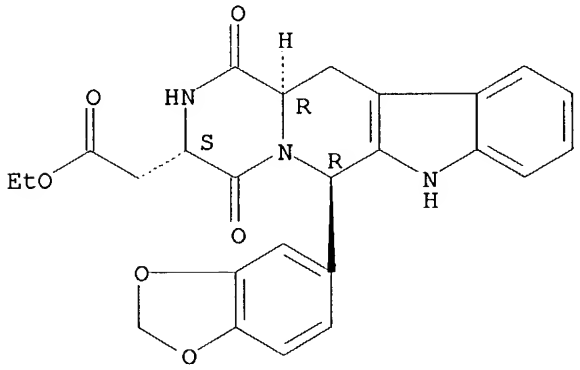
RN 395665-75-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, heptyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



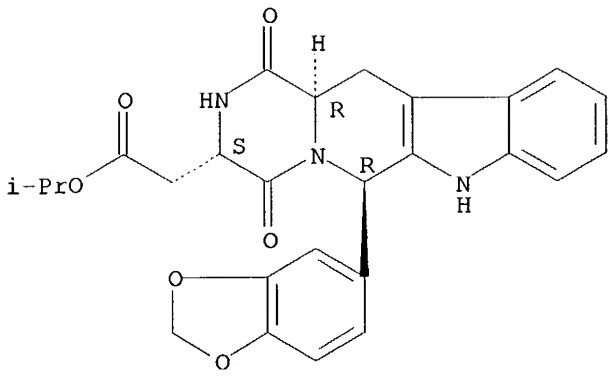
RN 395665-76-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, ethyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



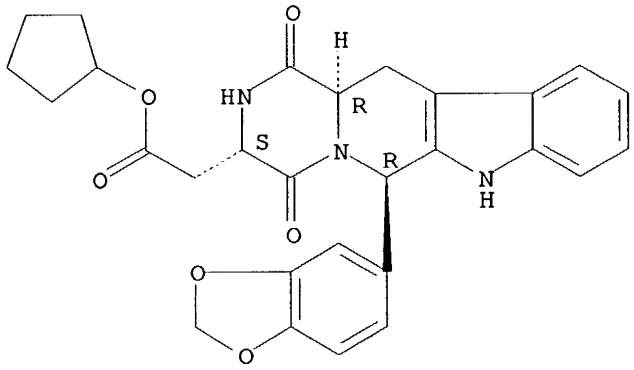
RN 395665-77-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, 1-methylethyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



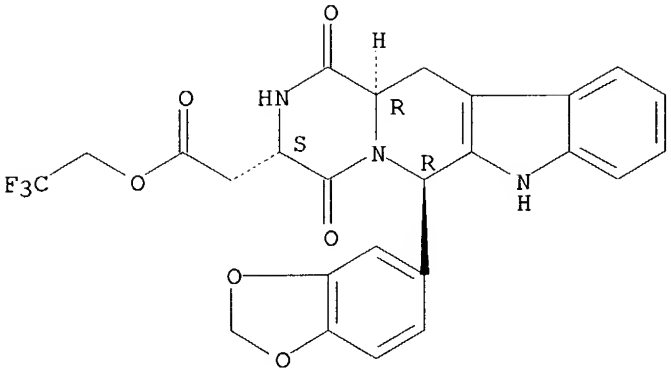
RN 395665-78-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, cyclopentyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



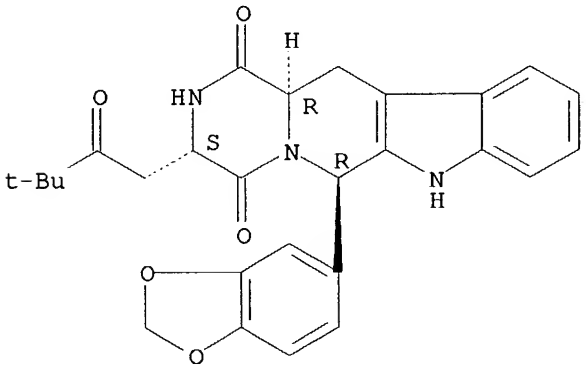
RN 395665-79-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, 2,2,2-trifluoroethyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



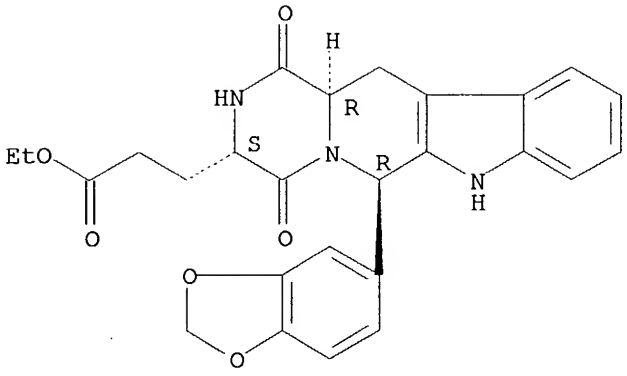
RN 395665-80-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-3-(3,3-dimethyl-2-oxobutyl)-2,3,6,7,12,12a-hexahydro-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



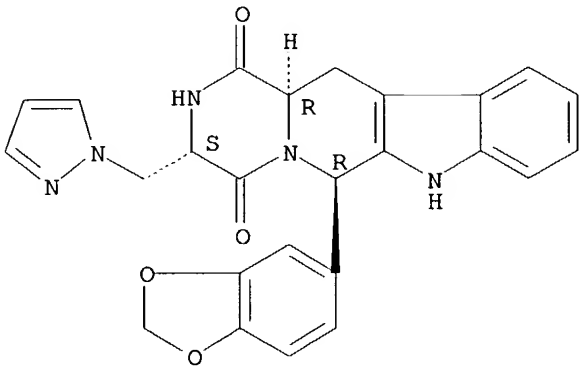
RN 395665-81-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-propanoic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-, ethyl ester, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



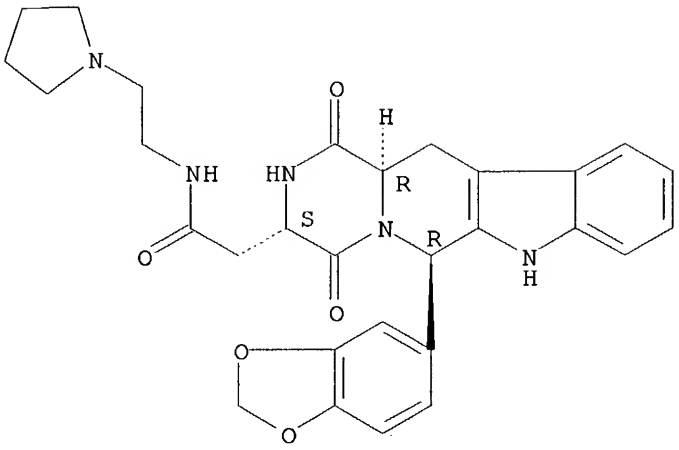
RN 395665-91-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-(1H-pyrazol-1-ylmethyl)-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



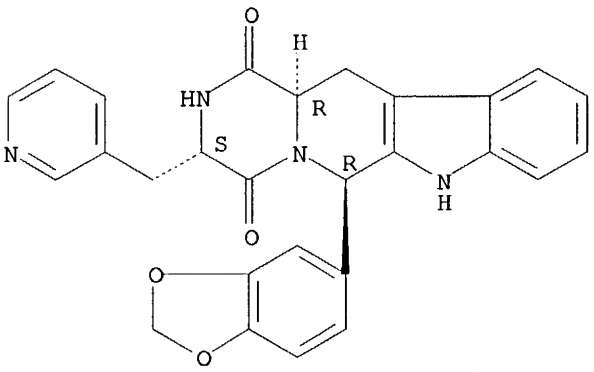
RN 395665-95-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-3-acetamide, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-1,4-dioxo-N-[2-(1-pyrrolidinyl)ethyl]-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



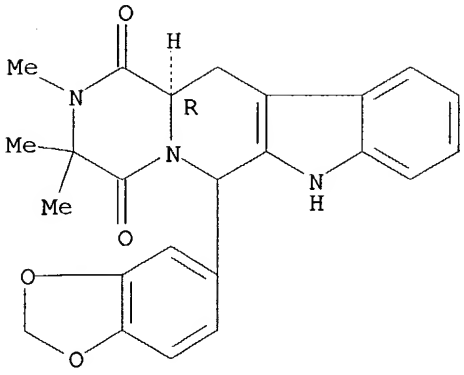
RN 395665-96-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-(3-pyridinylmethyl)-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 395665-98-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3,3-trimethyl-, (12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



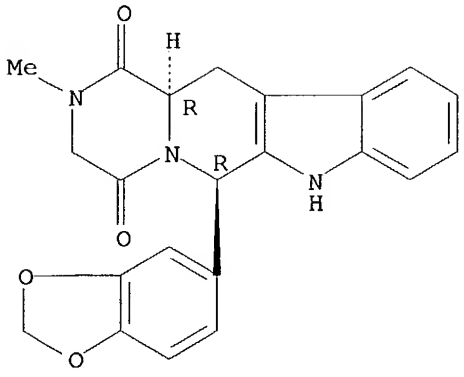
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 51 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:51273 CAPLUS
DN 136:96099
TI Treatment of male sexual dysfunction
IN Naylor, Alasdair Mark; Van der Graaf, Pieter Hadewijn; Wayman, Christopher Peter
PA Pfizer Limited, UK; Pfizer Inc.
SO PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002003995	A2	20020117	WO 2001-IB1187	20010702
	WO 2002003995	A3	20020418		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002052370	A1	20020502	US 2001-893585	20010628
	EP 1296687	A2	20030402	EP 2001-947709	20010702
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	GB 2000-16684	A	20000706		
	GB 2000-30647	A	20001215		
	GB 2001-6167	A	20010313		
	GB 2001-8483	A	20010404		
	US 2000-219100P	P	20000718		
	GB 2001-1584	A	20010122		
	US 2001-274957P	P	20010312		
	WO 2001-IB1187	W	20010702		

OS MARPAT 136:96099
AB The present invention relates to the use of neutral endopeptidase inhibitors (NEPi) and a combination of NEPi and phosphodiesterase type (PDE5) inhibitor for the treatment of male sexual dysfunction, in particular MED.
IT **171596-29-5,** IC-351
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of male sexual dysfunction using neutral endopeptidase inhibitors and their combination with phosphodiesterase type 5 inhibitors and other agents in relation to inhibition of angiotensin converting enzyme)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).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L5 ANSWER 52 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:10475 CAPLUS
DN 136:85828
TI Preparation of pyrazinopyridoindolediones as cyclic GMP phosphodiesterase inhibitors
IN Orme, Mark W.; Sawyer, Jason Scott; Schultze, Lisa M.; Daugan, Alain Claude-Marie; Gellibert, Francoise
PA Lilly Icos LLC, USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002000656	A2	20020103	WO 2001-US15935	20010515
	WO 2002000656	A3	20031002		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1366049	A2	20031203	EP 2001-935629	20010515
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003225094	A1	20031204	US 2002-297682	20021206
PRAI	US 2000-213647P	P	20000623		
	WO 2001-US15935	W	20010515		

OS MARPAT 136:85828
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The pyrazinopyridoindolediones I (R = halo, C1-6-alkyl; R1 = aryl, heteroaryl, amino, R4O, R4CO, R4SO, R4SO2, C1-4-alkylene-CO2R4, C1-4-alkylenehetreroaryl, sulfamoyl, cyano, NO2, CO-C1-4-alkyleneheteroaryl, C1-4-alkylene-OR4, etc.; R2 = monocyclic arom. ring consisting of benzene, thiophene, furan, and pyridine, and an optionally substituted bicyclic ring wherein the fused ring is a 5- or 6-membered ring comprised of C and optionally heteroatoms selected from O, S, and N; R3 = H, C1-6-alkyl; R4 = H, alkyl, aryl, heteroaryl, etc.) and their salts and solvates were prepd. as cyclic GMP phosphodiesterase inhibitors. Thus, D-tryptophan Me ester hydrochloride was treated with piperonal to give the carbolinecarboxylate II, which was treated with chloroacetyl chloride followed by cyclization with hydroxylamine-HCl to give the pyrazinopyridoindolediones III. The cyclic GMP phosphodiesterase inhibitor IC50 of III 0.0075 .mu.M.

IT **385769-78-8P 385769-80-2P 385769-82-4P**
385769-84-6P 385769-86-8P 385769-88-0P
385769-90-4P 385769-94-8P 385769-98-2P
385770-00-3P 385770-01-4P 385770-03-6P

385770-04-7P 385770-06-9P 385770-07-0P
385770-09-2P 385770-11-6P 385770-13-8P
385770-15-0P 385770-18-3P 385770-20-7P
385770-22-9P 385770-24-1P 385770-26-3P
385770-28-5P 385770-29-6P 385770-30-9P
385770-31-0P 385770-32-1P 385770-34-3P
385770-36-5P 385770-38-7P 385770-40-1P
385770-41-2P 385770-43-4P 385770-44-5P
385770-46-7P 385770-48-9P 385770-49-0P
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385770-56-9P 385770-57-0P 385770-58-1P
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385770-66-1P 385770-68-3P 385770-70-7P
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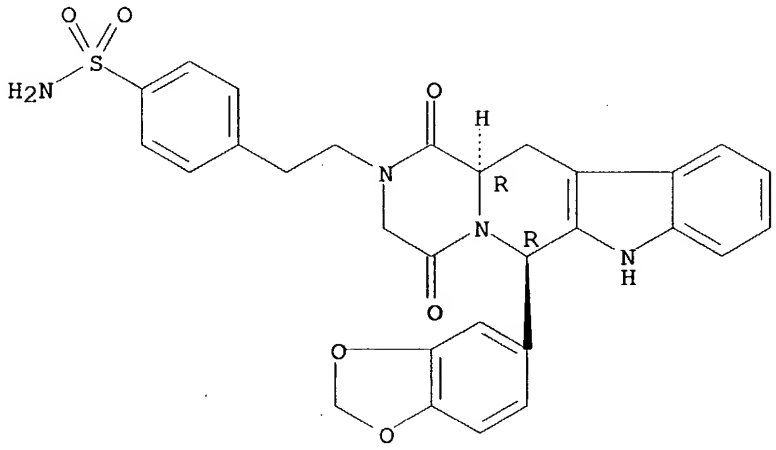
385770-76-3P 385770-77-4P 385770-78-5P
385770-79-6P 385770-80-9P 385770-82-1P
385770-83-2P 385770-85-4P 385770-89-8P
385770-91-2P 385770-92-3P 385770-93-4P
385770-95-6P 385770-96-7P 385770-98-9P
385770-99-0P 385771-02-8P 385771-03-9P
385771-05-1P 385771-06-2P 385771-08-4P
385771-10-8P
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrazinopyridoindolediones as cyclic GMP phosphodiesterase inhibitors)

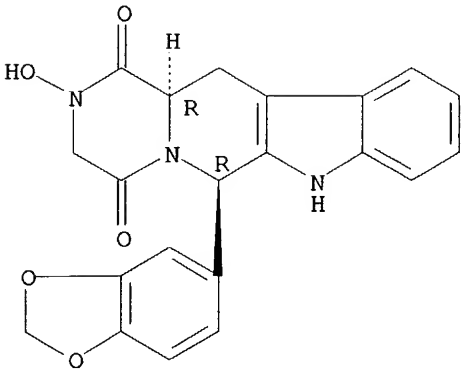
RN 385769-78-8 CAPLUS
CN Benzenesulfonamide, 4-[2-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



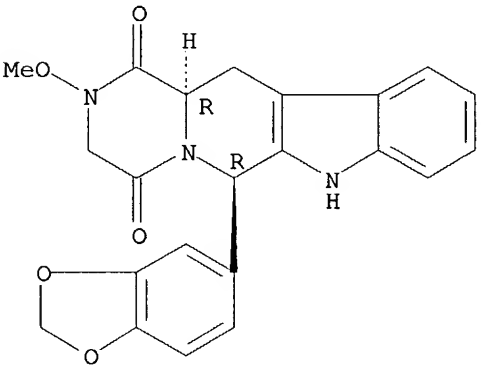
RN 385769-80-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-hydroxy-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



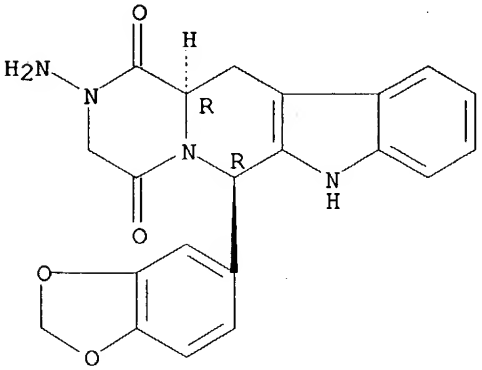
RN 385769-82-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methoxy-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



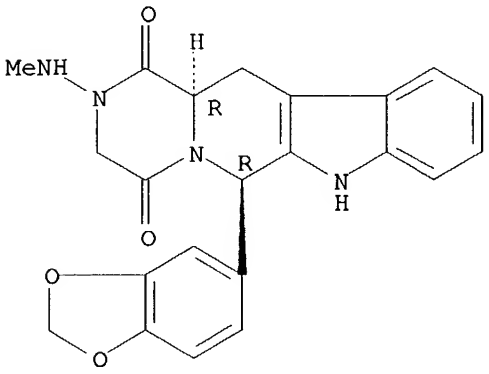
RN 385769-84-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-amino-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



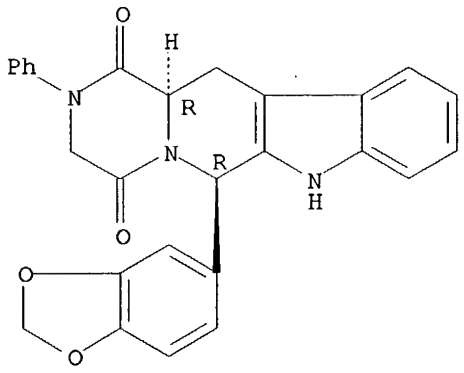
RN 385769-86-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(methylamino)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



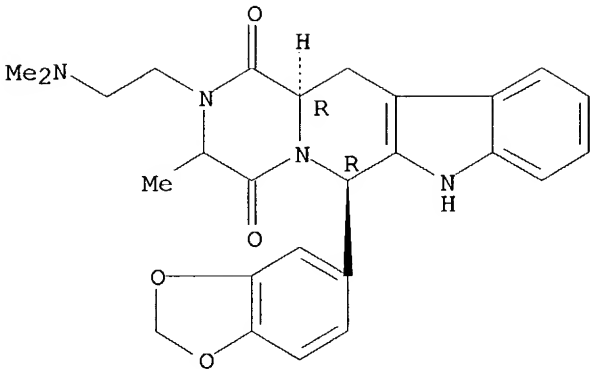
RN 385769-88-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-phenyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



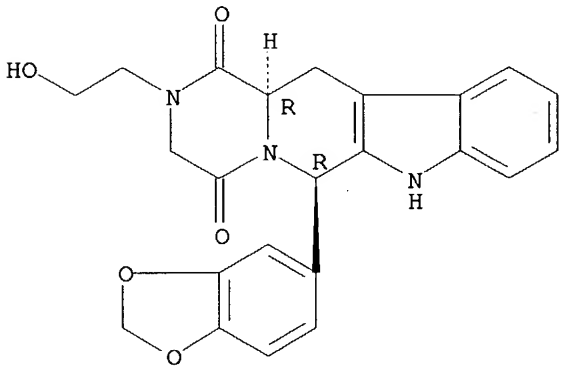
RN 385769-90-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-(dimethylamino)ethyl]-2,3,6,7,12,12a-hexahydro-3-methyl-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



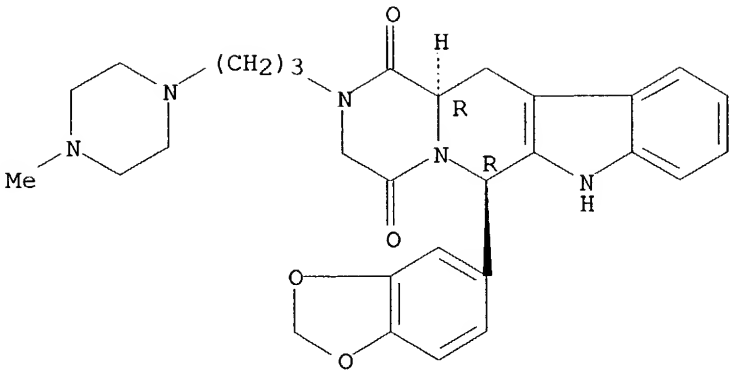
RN 385769-94-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-hydroxyethyl)-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



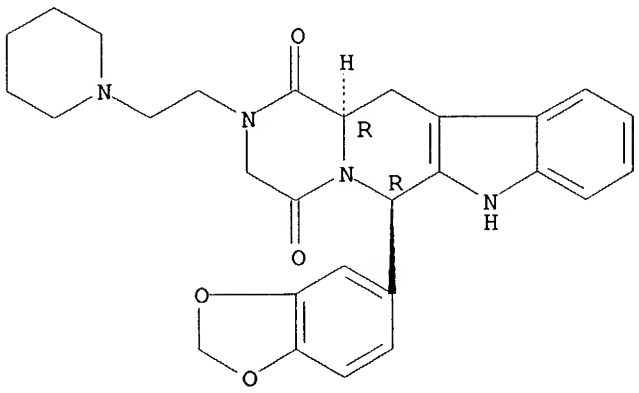
RN 385769-98-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[3-(4-methyl-1-piperazinyl)propyl]-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



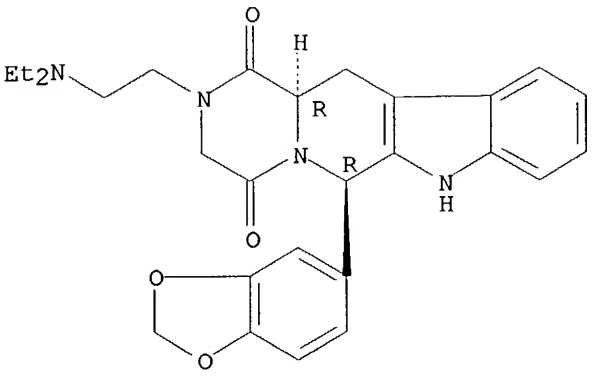
RN 385770-00-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(1-piperidinyl)ethyl]-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



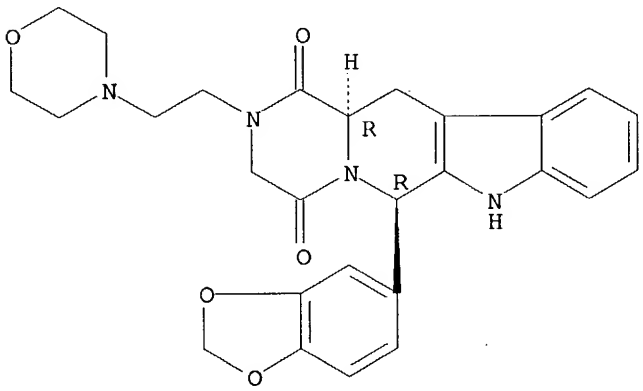
RN 385770-01-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-(diethylamino)ethyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



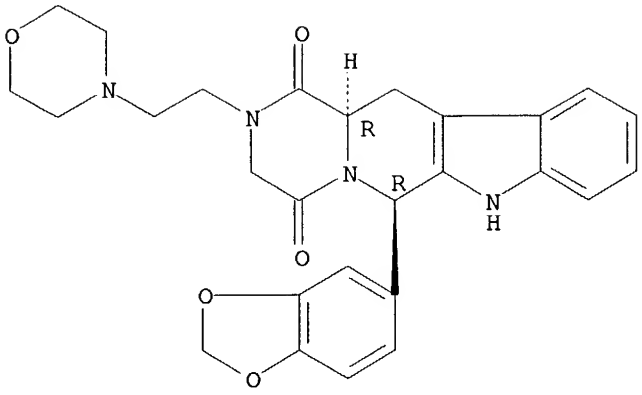
RN 385770-03-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(4-morpholinyl)ethyl]-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



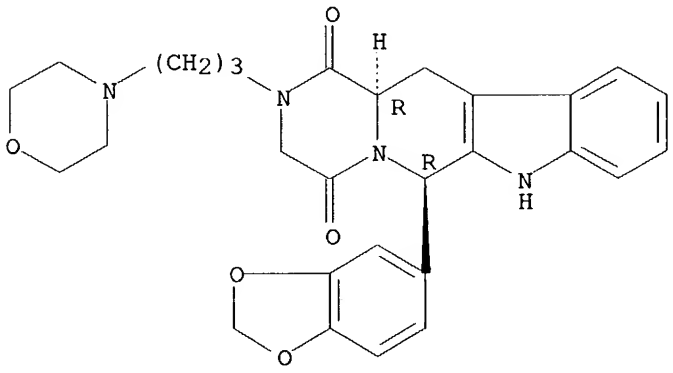
RN 385770-04-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(4-morpholinyl)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



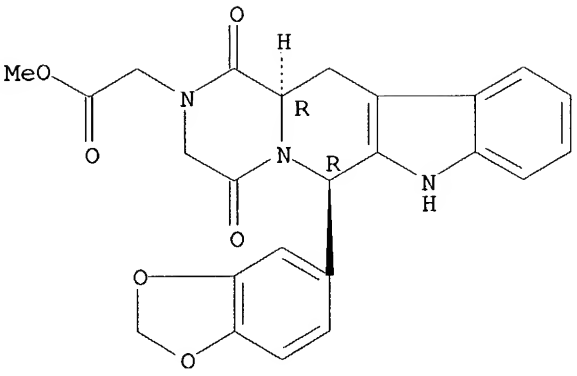
RN 385770-06-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[3-(4-morpholinyl)propyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



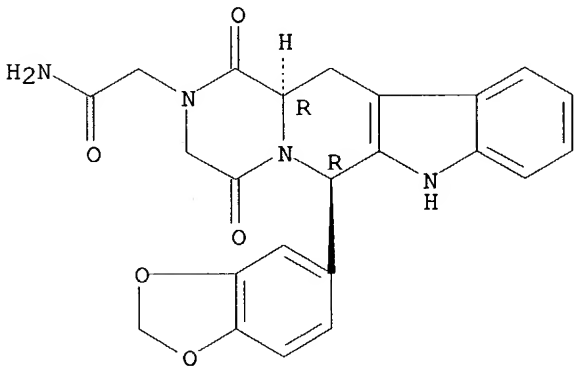
RN 385770-07-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, methyl ester, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



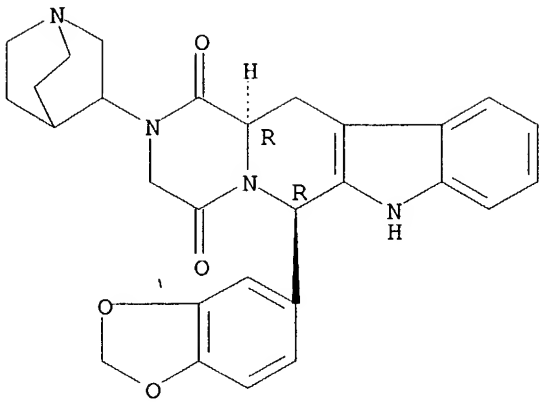
RN 385770-09-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetamide, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



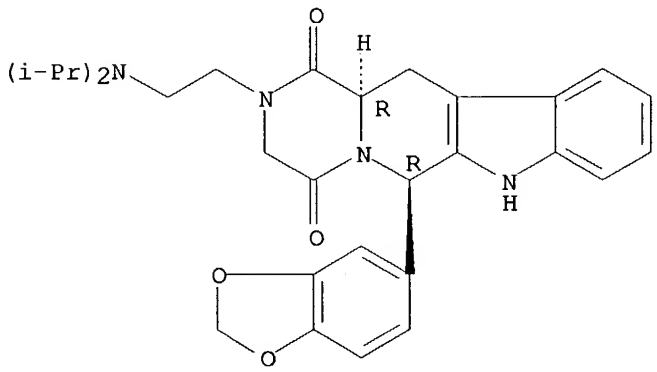
RN 385770-11-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-(1-azabicyclo[2.2.2]oct-3-yl)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



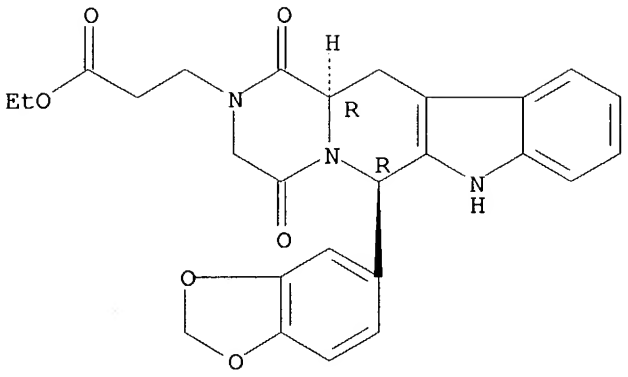
RN 385770-13-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-[bis(1-methylethyl)amino]ethyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



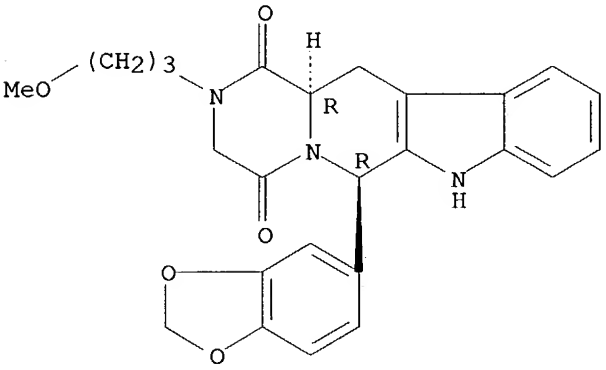
RN 385770-15-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanoic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, ethyl ester, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



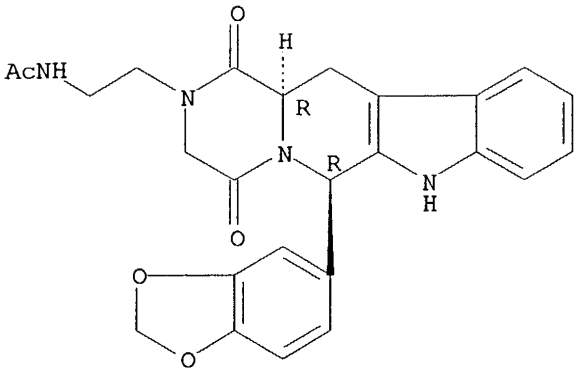
RN 385770-18-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(3-methoxypropyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



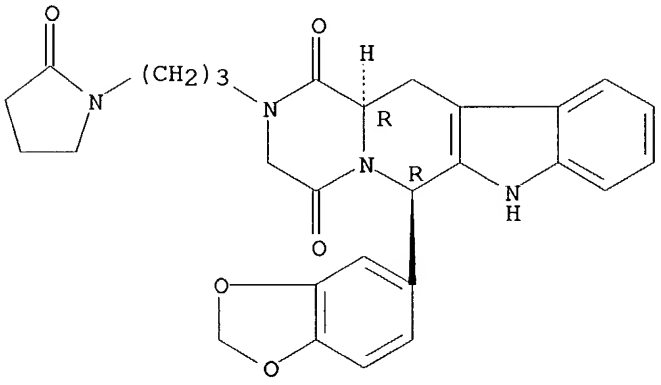
RN 385770-20-7 CAPLUS
CN Acetamide, N-[2-[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



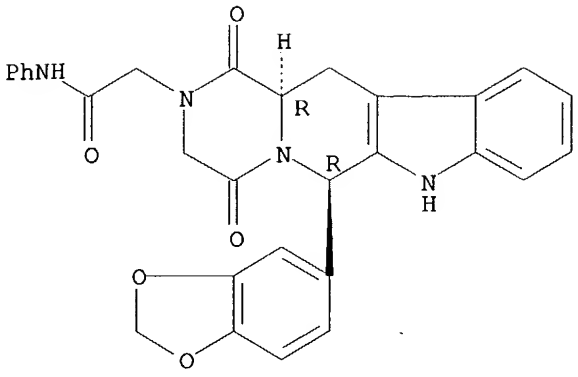
RN 385770-22-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[3-(2-oxo-1-pyrrolidinyl)propyl]-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



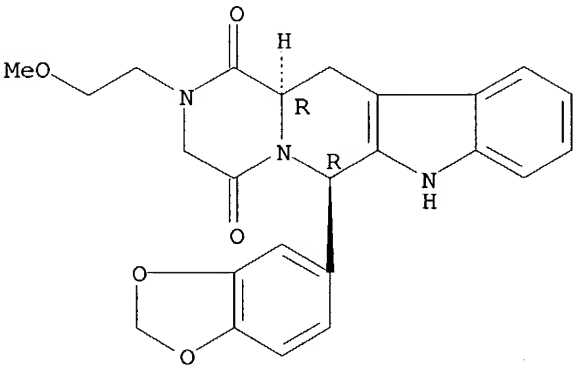
RN 385770-24-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetamide, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-N-phenyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



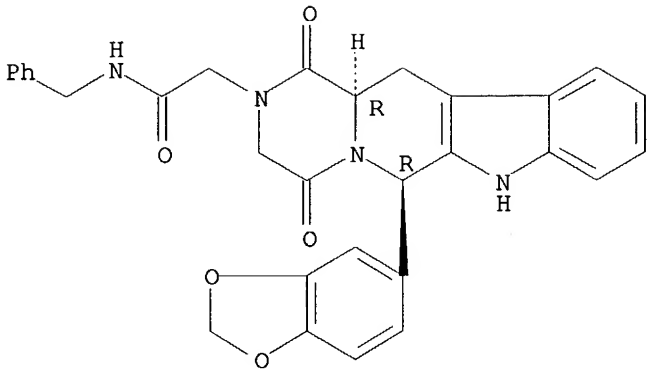
RN 385770-26-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-methoxyethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



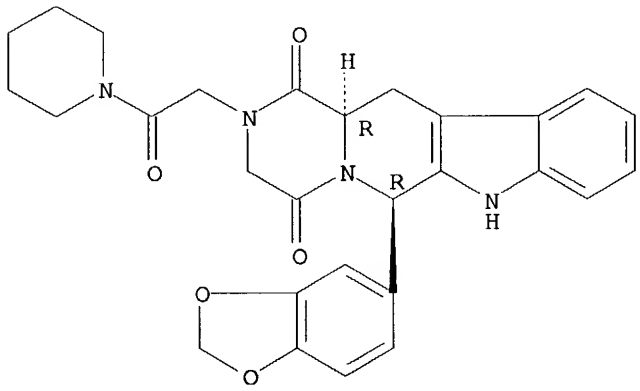
RN 385770-28-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetamide, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-N-(phenylmethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



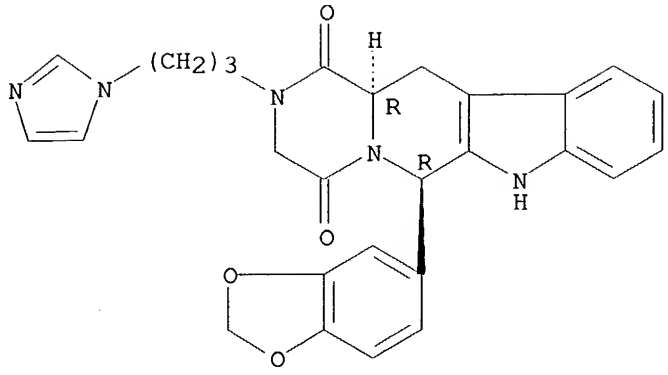
RN 385770-29-6 CAPLUS
CN Piperidine, 1-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



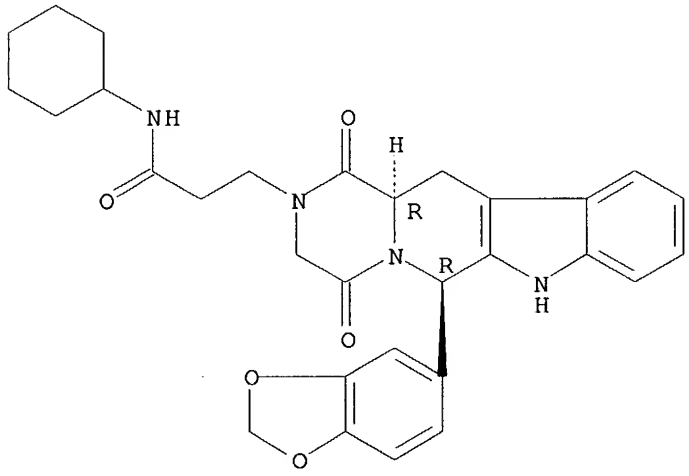
RN 385770-30-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[3-(1H-imidazol-1-yl)propyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



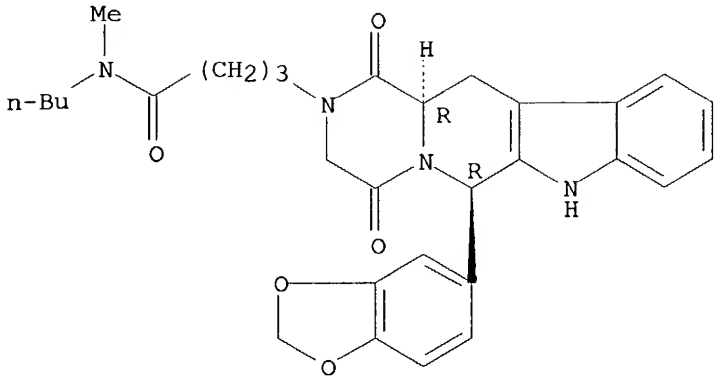
RN 385770-31-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanamide, 6-(1,3-benzodioxol-5-yl)-N-cyclohexyl-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



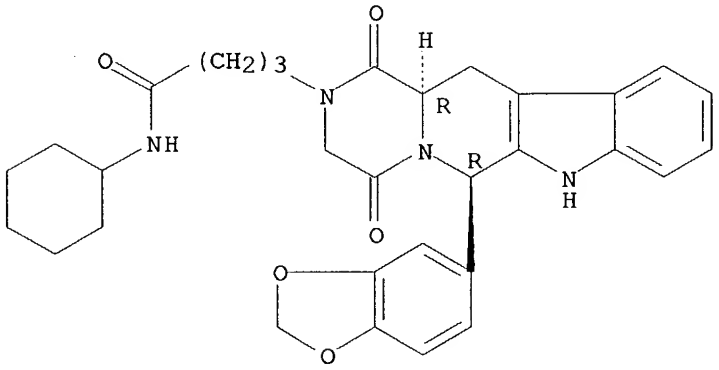
RN 385770-32-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-butanamide, 6-(1,3-benzodioxol-5-yl)-N-butyl-3,4,6,7,12,12a-hexahydro-N-methyl-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



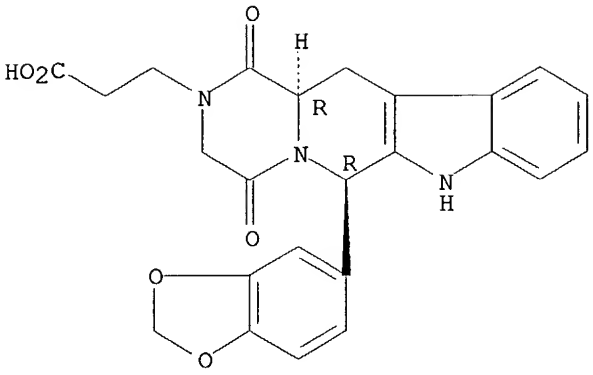
RN 385770-34-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-butanamide, 6-(1,3-benzodioxol-5-yl)-N-cyclohexyl-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



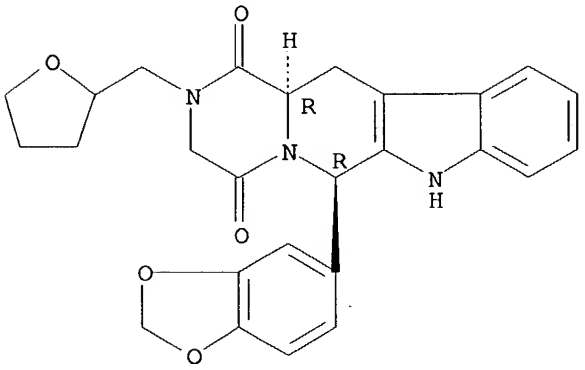
RN 385770-36-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanoic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



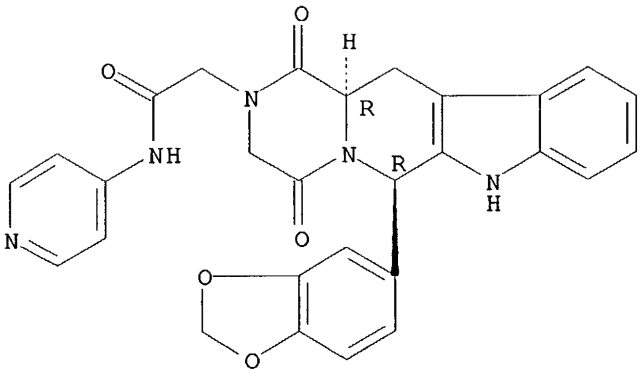
RN 385770-38-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(tetrahydro-2-furanyl)methyl]-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



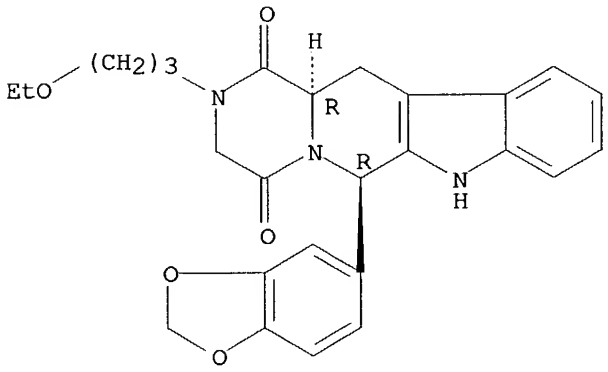
RN 385770-40-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetamide, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-N-4-pyridinyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



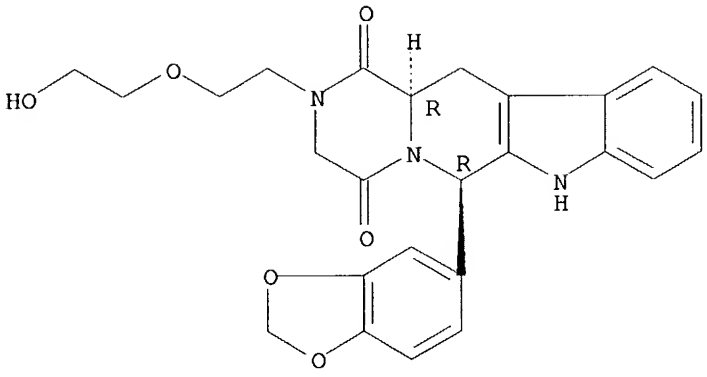
RN 385770-41-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(3-ethoxypropyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



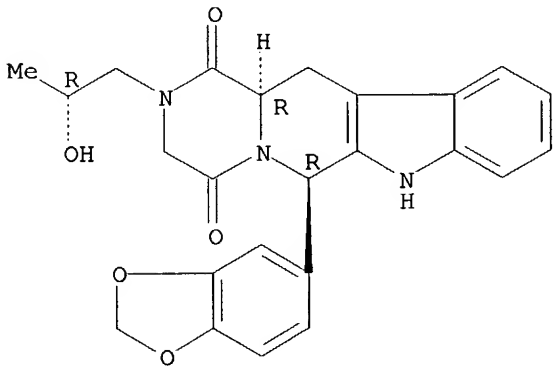
RN 385770-43-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(2-hydroxyethoxy)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



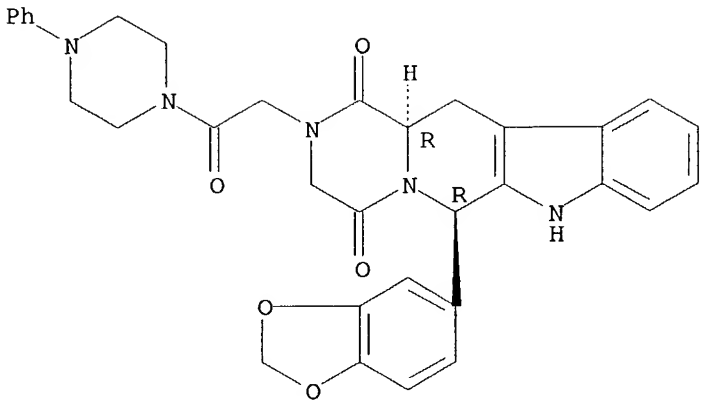
RN 385770-44-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(2R)-2-hydroxypropyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



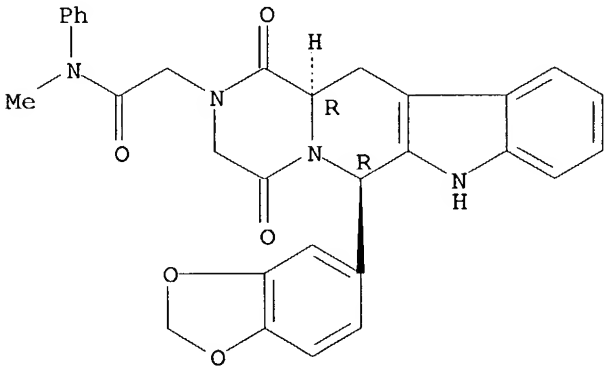
RN 385770-46-7 CAPLUS
CN Piperazine, 1-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]acetyl]-4-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



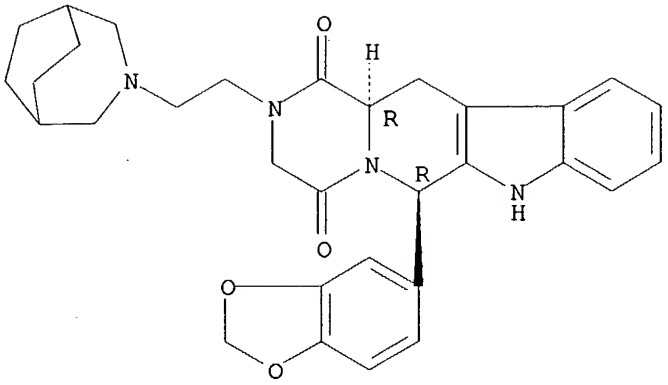
RN 385770-48-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetamide, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-N-methyl-1,4-dioxo-N-phenyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



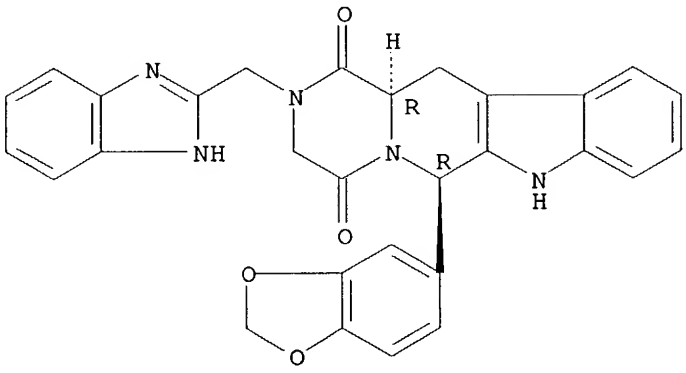
RN 385770-49-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-[2-(3-azabicyclo[3.2.2]non-3-yl)ethyl]-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



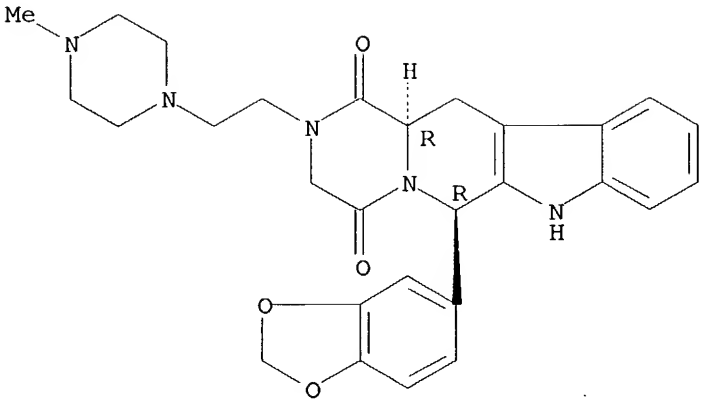
RN 385770-50-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-(1H-benzimidazol-2-ylmethyl)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



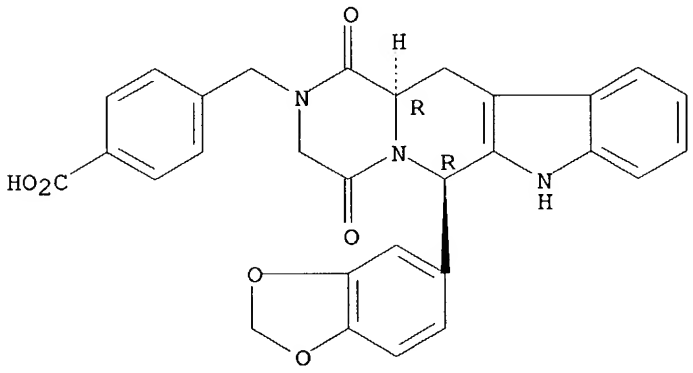
RN 385770-52-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(4-methyl-1-piperazinyl)ethyl]-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



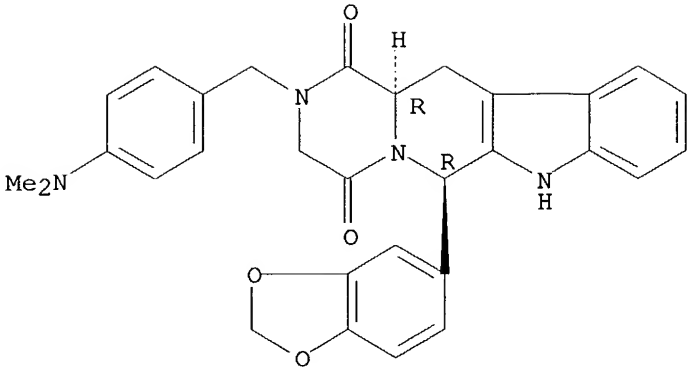
RN 385770-54-7 CAPLUS
CN Benzoic acid, 4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



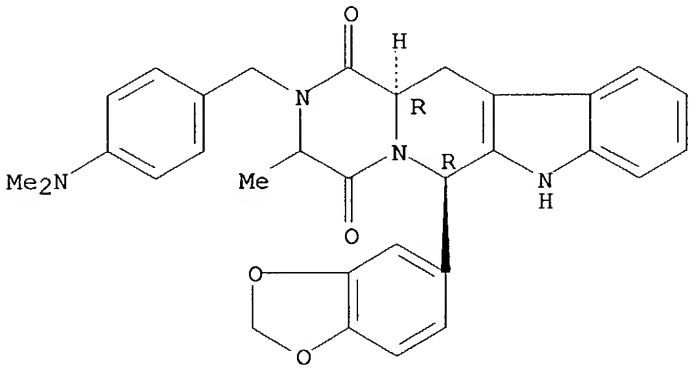
RN 385770-56-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[[4-(dimethylamino)phenyl]methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



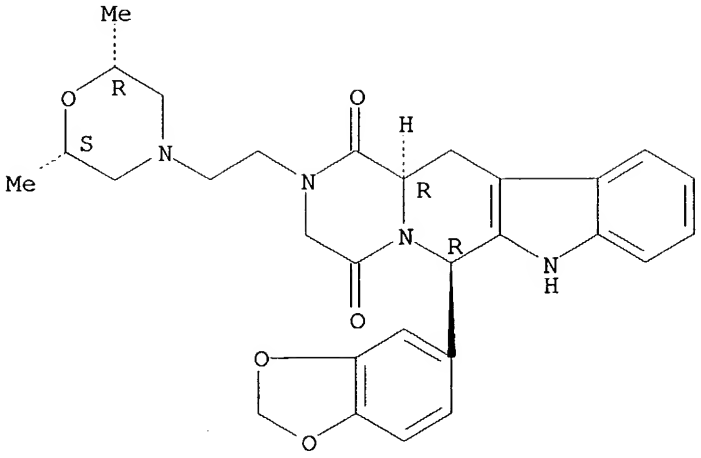
RN 385770-57-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[[4-(dimethylamino)phenyl]methyl]-2,3,6,7,12,12a-hexahydro-3-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



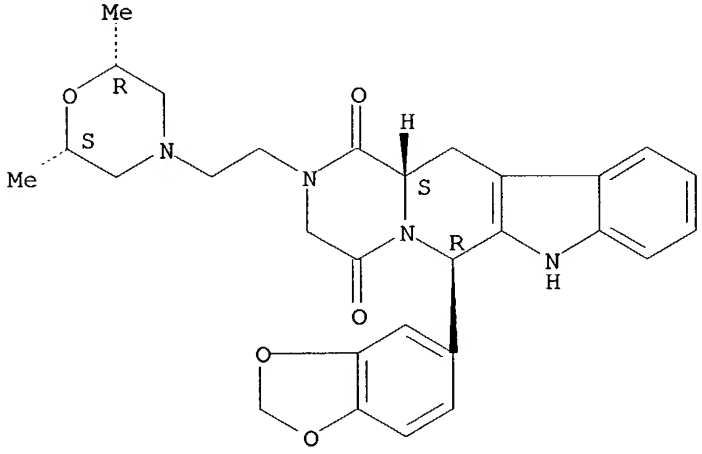
RN 385770-58-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-[(2R,6S)-2,6-dimethyl-4-morpholinyl]ethyl]-2,3,6,7,12,12a-hexahydro-, (6S,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



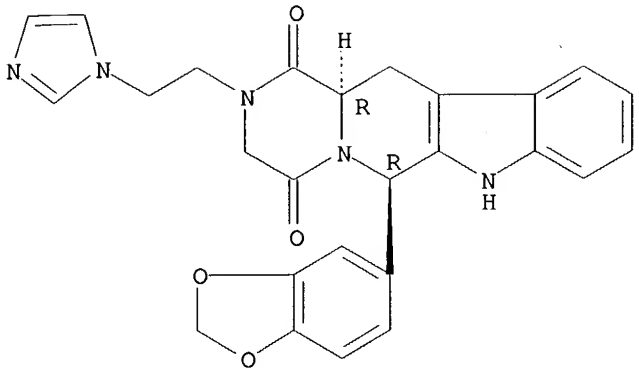
RN 385770-60-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-[(2R,6S)-2,6-dimethyl-4-morpholinyl]ethyl]-2,3,6,7,12,12a-hexahydro-, (6S,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



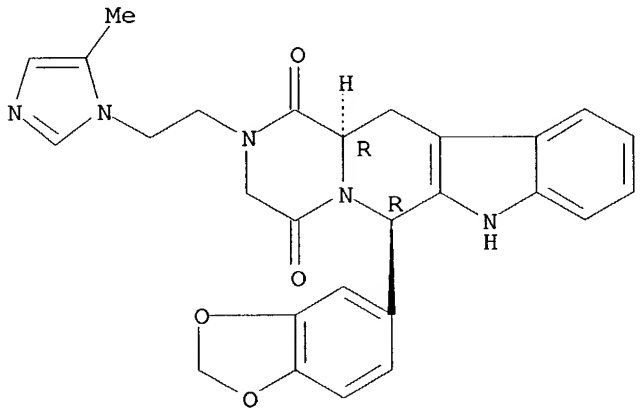
RN 385770-62-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(1H-imidazol-1-yl)ethyl]-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



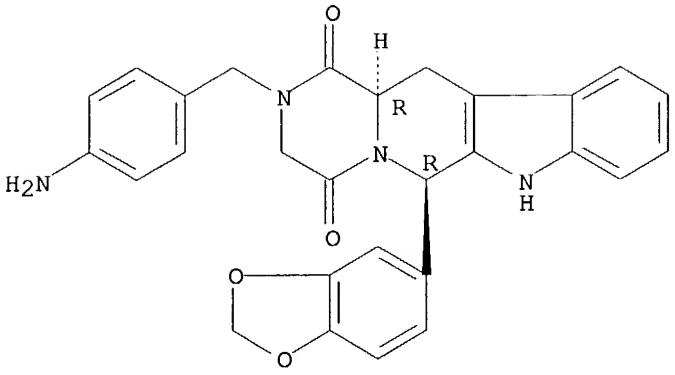
RN 385770-64-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(5-methyl-1H-imidazol-1-yl)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



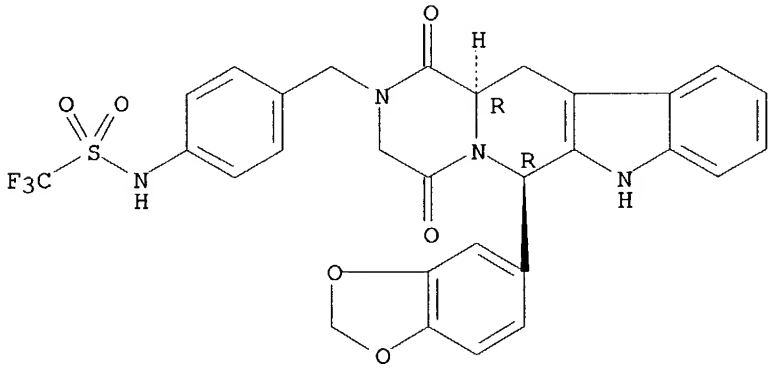
RN 385770-66-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-[(4-aminophenyl)methyl]-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



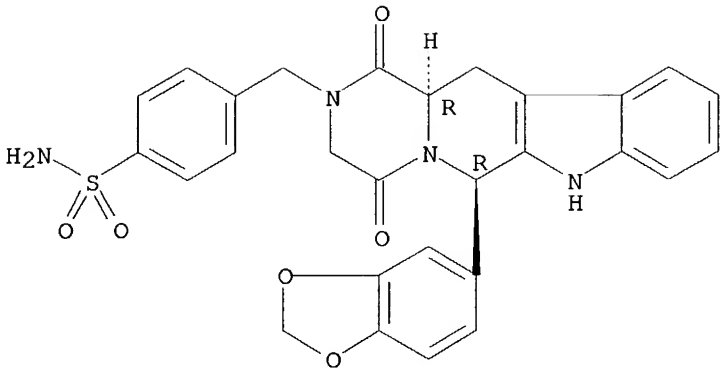
RN 385770-68-3 CAPLUS
CN Methanesulfonamide, N-[4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]phenyl]-1,1,1-trifluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



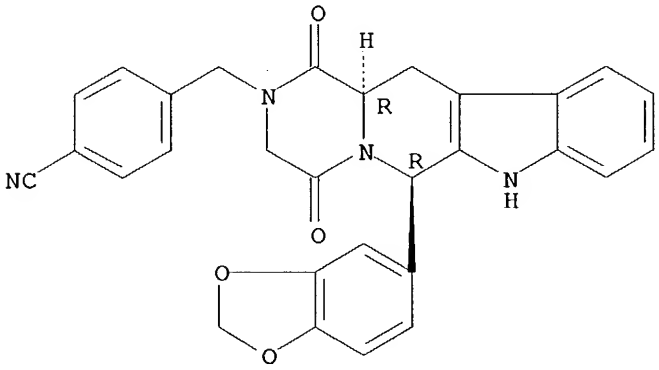
RN 385770-70-7 CAPLUS
CN Benzenesulfonamide, 4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



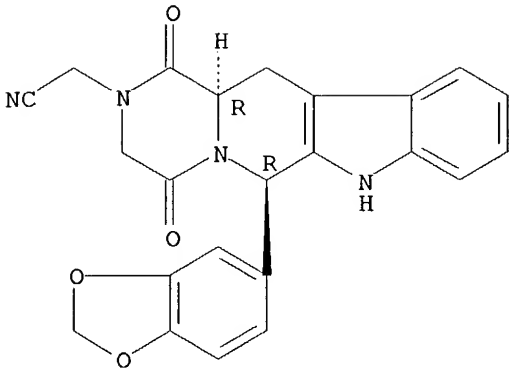
RN 385770-72-9 CAPLUS
CN Benzonitrile, 4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



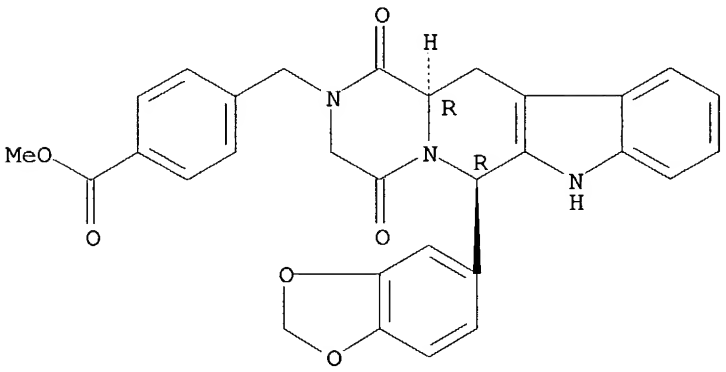
RN 385770-73-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetonitrile, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



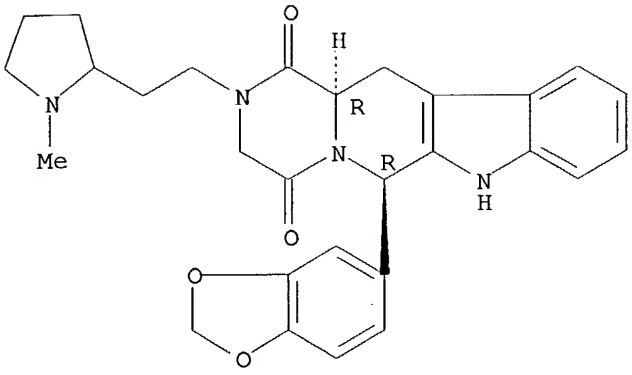
RN 385770-75-2 CAPLUS
CN Benzoic acid, 4-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



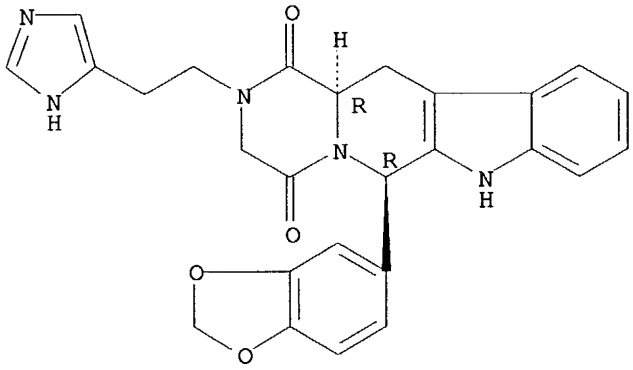
RN 385770-76-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(1-methyl-2-pyrrolidinyl)ethyl]-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



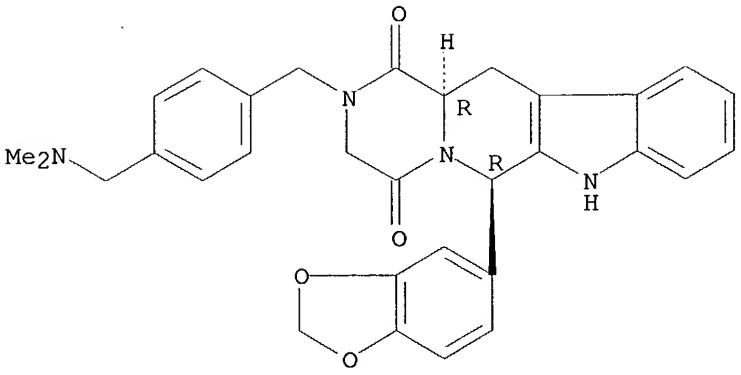
RN 385770-77-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(1H-imidazol-4-yl)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



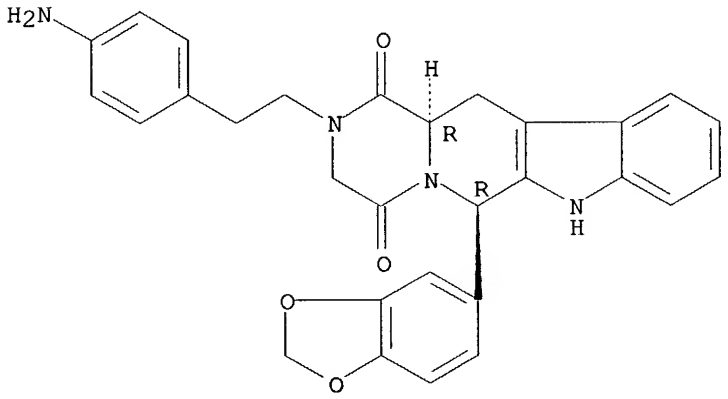
RN 385770-78-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[[4-[(dimethylamino)methyl]phenyl]methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



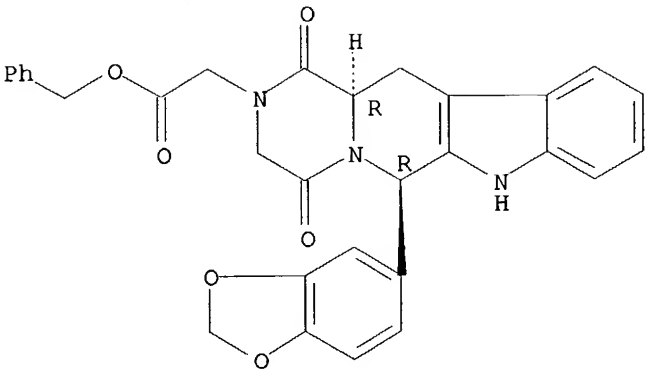
RN 385770-79-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-[2-(4-aminophenyl)ethyl]-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



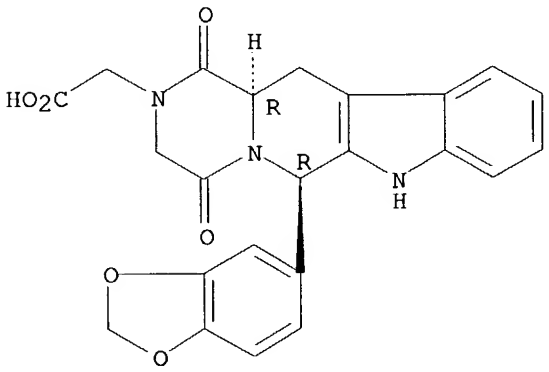
RN 385770-80-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, phenylmethyl ester, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



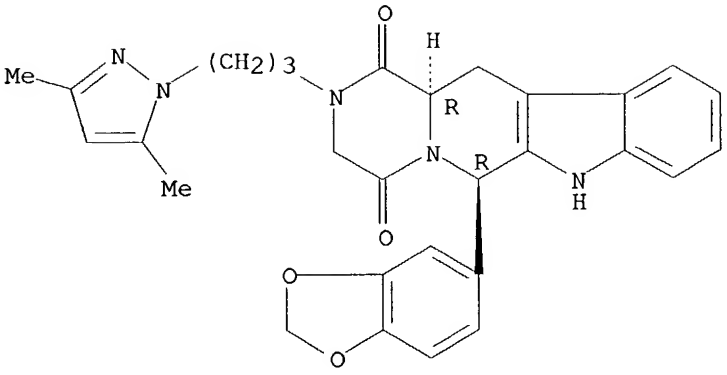
RN 385770-82-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



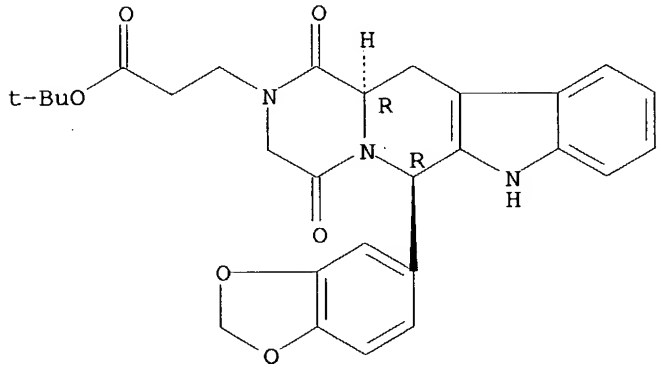
RN 385770-83-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[3-(3,5-dimethyl-1H-pyrazol-1-yl)propyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



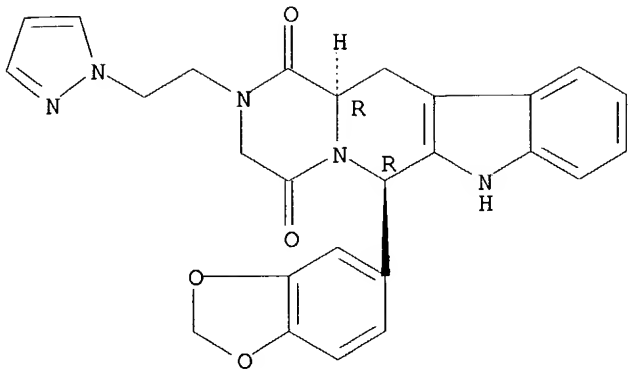
RN 385770-85-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-propanoic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, 1,1-dimethylethyl ester, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



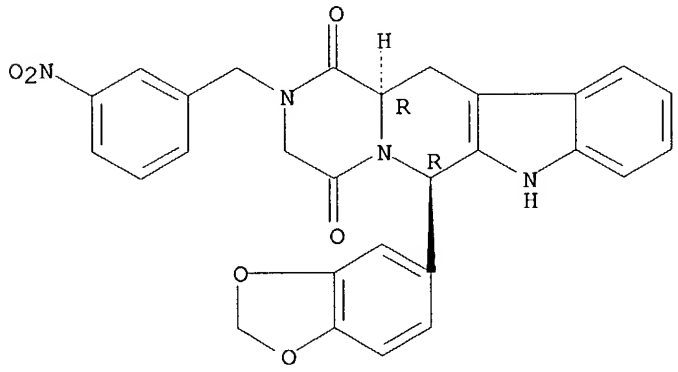
RN 385770-89-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(1H-pyrazol-1-yl)ethyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



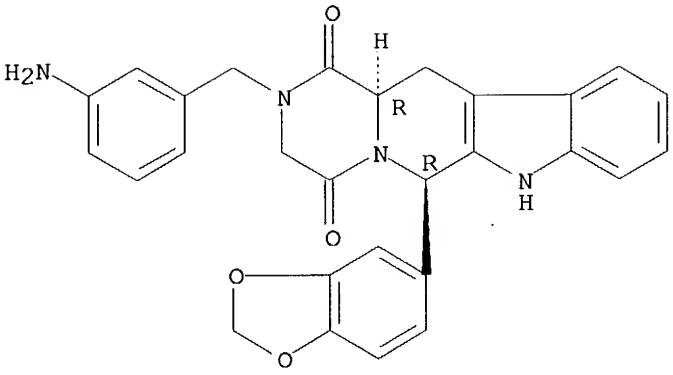
RN 385770-91-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(3-nitrophenyl)methyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



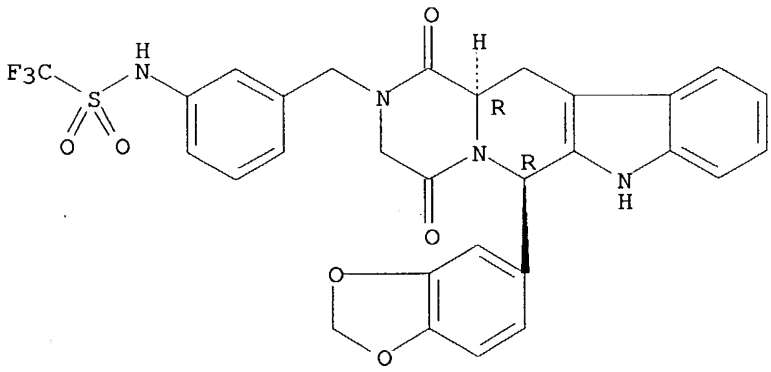
RN 385770-92-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 2-[(3-aminophenyl)methyl]-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



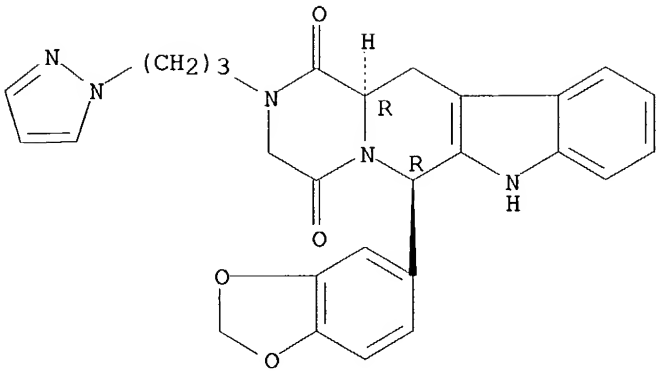
RN 385770-93-4 CAPLUS
CN Methanesulfonamide, N-[3-[[(6R,12aR)-6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxopyrazino[1',2':1,6]pyrido[3,4-b]indol-2(1H)-yl]methyl]phenyl]-1,1,1-trifluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



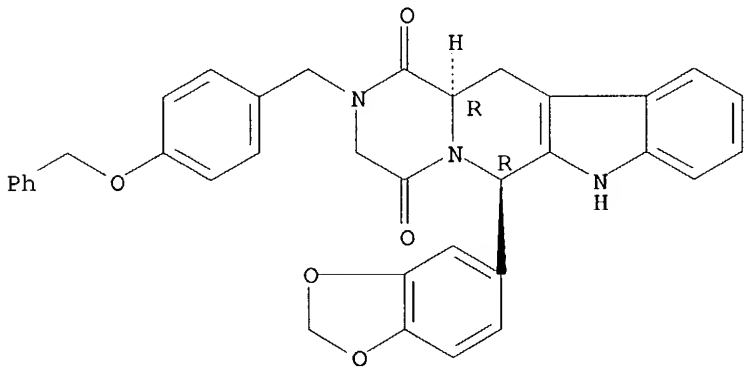
RN 385770-95-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[3-(1H-pyrazol-1-yl)propyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



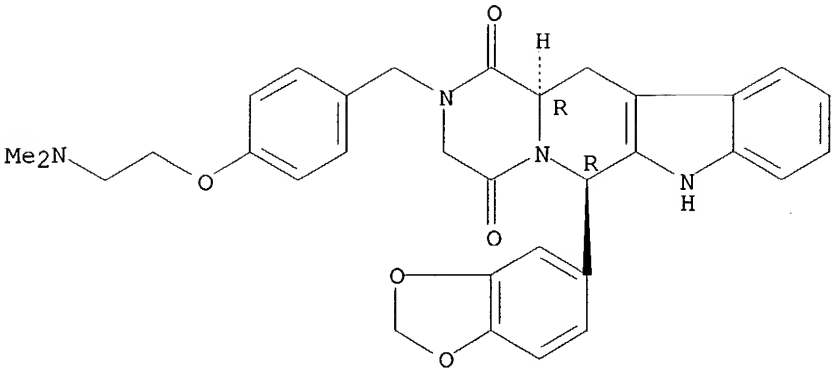
RN 385770-96-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[[4-(phenylmethoxy)phenyl]methyl]-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



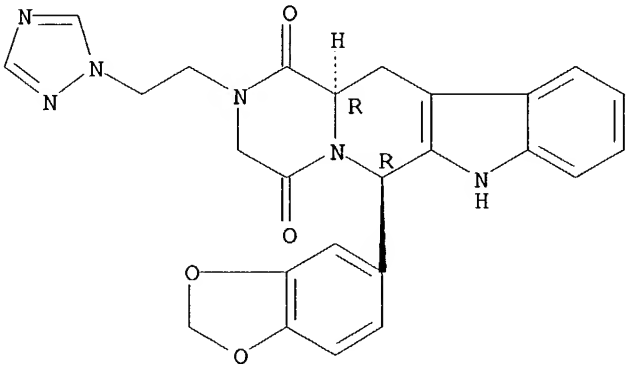
RN 385770-98-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[[4-[2-(dimethylamino)ethoxy]phenyl]methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



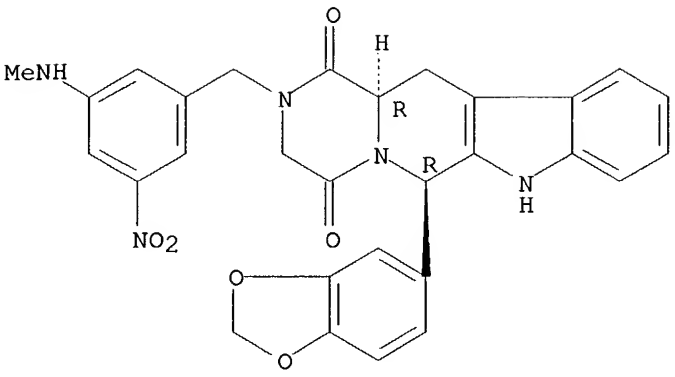
RN 385770-99-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(1H-1,2,4-triazol-1-yl)ethyl]-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



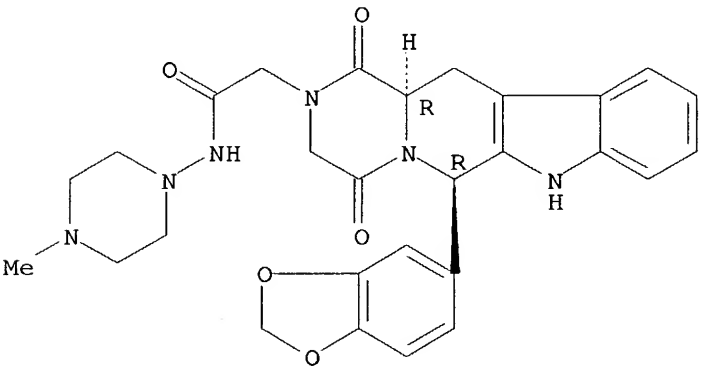
RN 385771-02-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[[3-(methylamino)-5-nitrophenyl]methyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



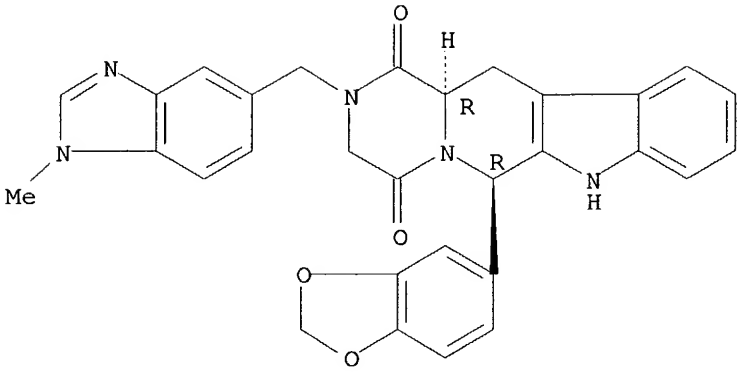
RN 385771-03-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetamide, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-N-(4-methyl-1-piperazinyl)-1,4-dioxo-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



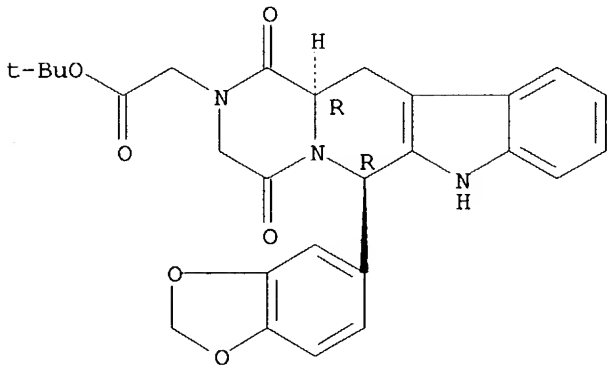
RN 385771-05-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[(1-methyl-1H-benzimidazol-5-yl)methyl]-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



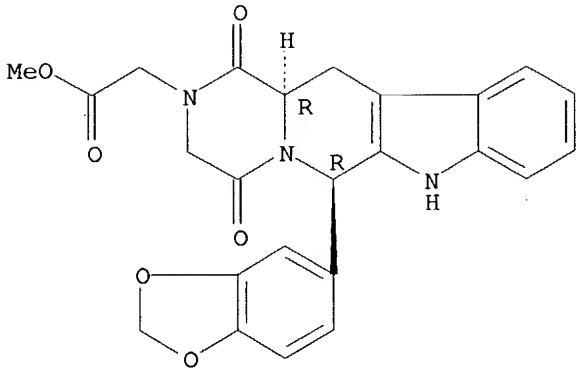
RN 385771-06-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, 1,1-dimethylethyl ester, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



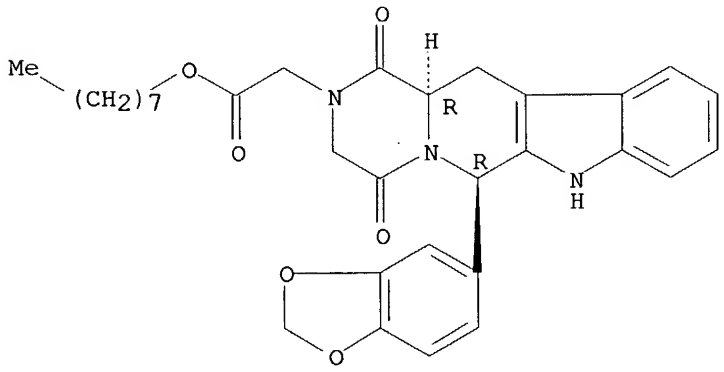
RN 385771-08-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, methyl ester, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 385771-10-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-2(1H)-acetic acid, 6-(1,3-benzodioxol-5-yl)-3,4,6,7,12,12a-hexahydro-1,4-dioxo-, octyl ester, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 53 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:924320 CAPLUS
DN 136:31728
TI Daily treatment for erectile dysfunction using a phosphodiesterase 5 (PDE5) inhibitor
IN Whitaker, John S.; Saenz de Tejada, Inigo; Ferguson, Kenneth M.
PA USA
SO U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 558,911.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

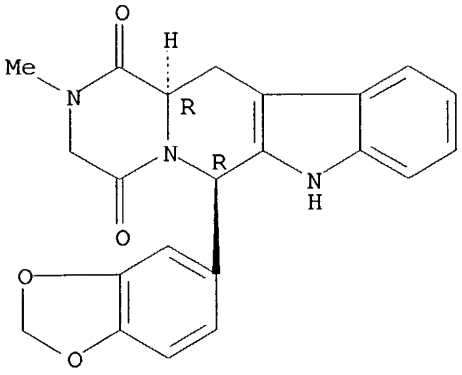
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2001053780	A1	20011220	US 2001-834442	20010413
	EP 1173181	A2	20020123	EP 2000-926367	20000426
	EP 1173181	B1	20031015		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6451807	B1	20020917	US 2000-558911	20000426
	JP 2002543116	T2	20021217	JP 2000-614984	20000426
	BR 2000010181	A	20030225	BR 2000-10181	20000426
	NZ 514882	A	20030829	NZ 2000-514882	20000426
	AT 251908	E	20031115	AT 2000-926367	20000426
	HR 2001000778	A1	20021231	HR 2001-778	20011023
	NO 2001005275	A	20011206	NO 2001-5275	20011029
	US 2003100478	A1	20030529	US 2002-198903	20020719
	US 2003144296	A1	20030731	US 2003-341664	20030114
PRAI	US 1999-132036P	P	19990430		
	US 2000-558911	A2	20000426		
	WO 2000-US11129	W	20000426		
	US 2001-834442	A3	20010413		

AB The invention provides phosphodiesterase (PDE) enzyme inhibitors and to their use in pharmaceutical articles of manuf. In particular, the invention provides potent inhibitors of cyclic guanosine 3',5'-monophosphate specific phosphodiesterase type 5 (PDE5) that, when incorporated into a pharmaceutical product at about 1-10 mg unit dosage, are useful for the treatment of sexual dysfunction by daily administration of the PDE5 inhibitor. The articles of manuf. described are characterized by PDE5 inhibition, and accordingly, provide a benefit in therapeutic areas where inhibition of PDE5 is desired, esp. erectile dysfunction, with minimization or elimination of adverse side effects resulting from inhibition of other phosphodiesterase enzymes and with an improvement of vascular conditioning.

IT **171596-29-5 171596-40-0**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 5 inhibitor for daily treatment for erectile dysfunction)

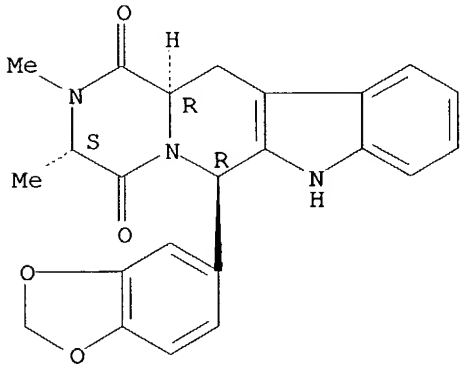
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 54 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:916407 CAPLUS
DN 136:53755
TI Synthesis of nitrosated and nitrosylated (hetero)cyclic phosphodiesterase inhibitors used in treatment of sexual dysfunction
IN Garvey, David S.; Saenz de Tejada, Inigo; Earl, Richard A.; Khanapure, Subhash P.
PA Nitromed, Inc., USA
SO U.S., 117 pp., Cont.-in-part of U.S. 5,958,926.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6331543	B1	20011218	US 1999-387727	19990901
	US 5874437	A	19990223	US 1996-740764	19961101
	WO 9819672	A1	19980514	WO 1997-US19870	19971031
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5958926	A	19990928	US 1998-145142	19980901
	US 2002019405	A1	20020214	US 2001-941691	20010830
	US 6462044	B2	20021008		
	US 2003023087	A1	20030130	US 2002-216886	20020813
PRAI	US 1996-740764	A2	19961101		
	WO 1997-US19870	A2	19971031		
	US 1998-145142	A2	19980901		
	US 1999-387727	A1	19990901		
	US 2001-941691	A3	20010830		

OS MARPAT 136:53755
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. I-V, derivs. thereof, and certain substituted Ph and phthalzaine derivs. were claimed [D2 = H, alkyl, D; D = NO, NO2, alkyl, acyl, phosphoryl, silyl, etc.; A1-3 comprise the other subunits of a 5- or 6-membered monocyclic arom. ring; R8 = H, (halo)alkyl; p = 1-10; R24 = H, cyclohexyl, piperidinyl, etc., with the proviso that at least one of A1-3, J, or R24 contains T-Q or D; T = bond, O, S(O), amino; Q = NO, NO2; D1 = D or H; R37 = (hetero)aryl; R38 = H, halo, alkyl; G1 = alkyl, alkenyl or is part of a ring fused to the piperidine moiety of III; G4 = O, S; R40 = H, alkyl, haloalkyl, halo, etc.; R41 = alkyl, hydroxyalkyl, alkylcarboxy, etc.; R42 = aryl, alkylaryl, alkyloxyaryl; T1 = alkyl, oxyalkyl, thioalkyl, aminoalkyl]. Two synthetic examples were provided. E.g., the S-nitroso deriv. of the 3-mercapto-3-methylbutyric acid ester of dipyridamole (VI) was prepd. in 4 steps from dipyridamole in 3.5% overall yield. VI at doses of 10 and 30 .mu.M was more efficacious in relaxing phenylephrine-induced tissue contraction than was the known phosphodiesterase inhibitor, dipyridamole. The present invention describes novel (nitrosated/nitrosylated) phosphodiesterase inhibitors, and compns. contg. at least one (nitrosated/nitrosylated) phosphodiesterase inhibitor, and, optionally, one or more compds. that donate, transfer or release NO, elevate endogenous levels of endothelium-derived relaxing factor, stimulate endogenous synthesis of NO,

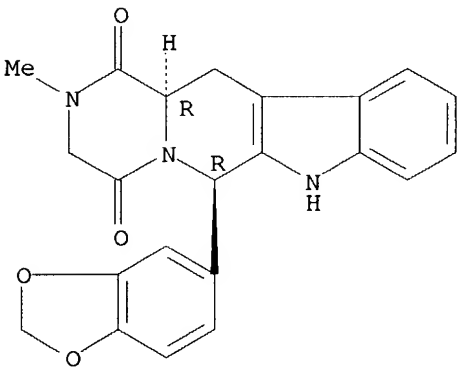
or is a substrate for nitric oxide synthase and/or one or more vasoactive agents. The present invention also provides methods for treating or preventing sexual dysfunctions in males and females, for enhancing sexual responses in males and females, and for treating or preventing diseases induced by the increased metab. of cGMP, such as hypertension, pulmonary hypertension, etc.

IT **171596-29-5D**, ICOS 351, nitroso derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis of nitrosated and nitrosylated (hetero)cyclic phosphodiesterase inhibitors used in treatment of sexual dysfunction)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

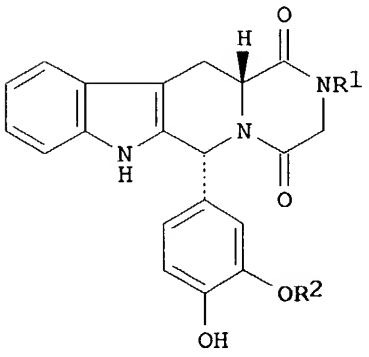


RE.CNT 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 55 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:904172 CAPLUS
DN 136:20091
TI Preparation of tetracyclic diketopiperazine compounds as PDE5 inhibitor
IN Orme, Mark W.; Daugan, Alain Claude-Marie; Bombrun, Agnes
PA Lilly Icos Llc, USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001094347	A1	20011213	WO 2001-US15937	20010515
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1289990	A1	20030312	EP 2001-945961	20010515
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003153575	A1	20030814	US 2002-296099	20021122
PRAI	US 2000-210324P	P	20000608		
	WO 2001-US15937	W	20010515		

OS MARPAT 136:20091
GI



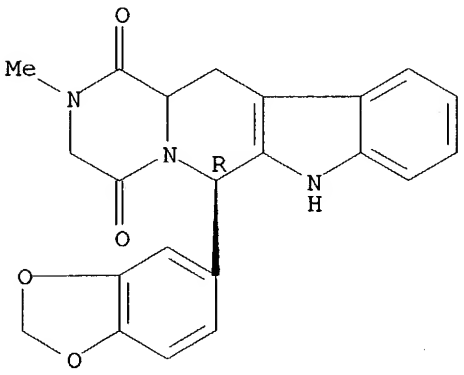
I

AB The title compds. I [R1 = C1-6 alkyl; R2 = H, Me] were prepd. and use of the compds. as PDE5 inhibitors was described.. E.g., (6R,12aR)-6-(3,4-dihydroxyphenyl)-2-methyl-2,3,6,7,12,12a-hexahydropyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione was prepd. I may be used for male erectile dysfunction or female arousal disorder.

IT **378788-17-1P**
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. of tetracyclic diketopiperazine compds. as PDE5 inhibitor)
RN 378788-17-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 56 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:904168 CAPLUS
DN 136:20090
TI Preparation of cyclic guanosine monophosphate specific phosphodiesterase inhibiting heterocyclylpyrazinopyridoindolediones for treatment of cardiovascular disorders and erectile disfunction
IN Orme, Mark W.; Sawyer, Jason Scott; Daugan, Alain Claud-Marie
PA Lilly Icos LLC, USA
SO PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001094345	A2	20011213	WO 2001-US15936	20010515
	WO 2001094345	A3	20020718		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1289989	A2	20030312	EP 2001-945960	20010515
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003225092	A1	20031204	US 2002-297245	20021203
PRAI	US 2000-210137P	P	20000607		
	WO 2001-US15936	W	20010515		

OS MARPAT 136:20090
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

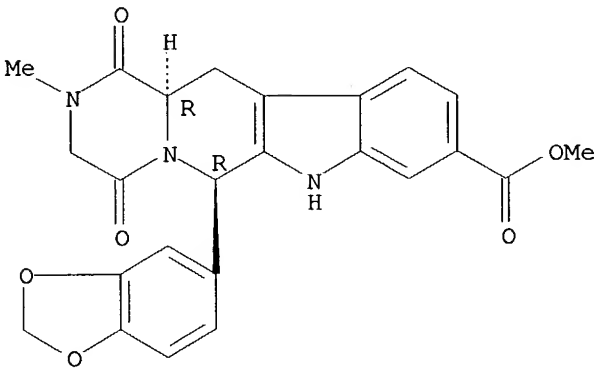
AB The pyrazinopyridoindolediones I [R1 = H, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, heterocycloalkyl, etc; R2 = (un)substituted Ph, thienyl, furanyl, pyridyl, bicyclic ring optionally contg. O, S, N hetero atoms, e.g. benzodioxolyl; R3 = H, alkyl; R4 = aryl, heteroaryl, cycloalkyl, acyl, acyloxy, alkoxycarbonyl, aminoalkyl, carbamoyl, alkoxy, amino, acylamino, nitro, cyano, alkylthio etc.; R5 = H, halo, alkyl; R4R5 = 5-, 6-, 7-membered ring optionally contg. O, S, N atoms; m = 1, 2, 3] and their diastereoisomers and pharmaceutically acceptable salts were prepd., possessed cGMP specific phosphodiesterase inhibiting activity, and were useful in the treatment of various cardiovascular disorders, erectile disfunction, and female sexual arousal disorder. Thus, the Me ester of 5-hydroxytryptophan condensed with piperonal in trifluoroacetic acid/CH2Cl2 to give the [(methylenedioxy)phenyl]pyridoindole II which was acylated by ClCH2COCl and then cyclized with MeNH2 to give the [(methylenedioxy)phenyl]hexahydropyrazinopyridoindoledione III that inhibited cGMP specific phosphodiesterase in vitro with an IC50 of 48.1 nM.
IT **379234-97-6P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of (benzodioxolyl)pyrazinopyridoindolediones with cGMP-specific phosphodiesterase inhibiting activity useful in treating cardiovascular, erectile, and female sexual arousal disorders)

RN 379234-97-6 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-9-carboxylic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxo-, methyl ester, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

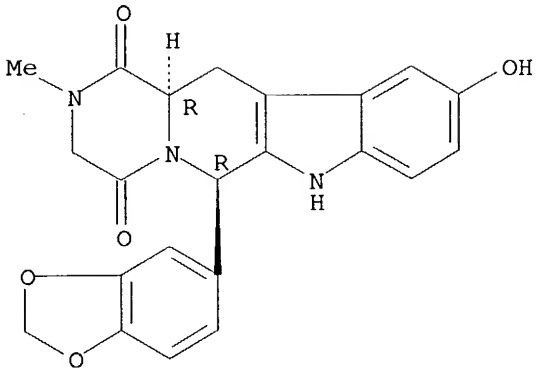


IT **379234-74-9P 379234-78-3P 379234-82-9P**
379234-88-5P 379234-98-7P 379235-06-0P
379235-11-7P 379235-12-8P 379235-13-9P
379235-15-1P 379235-16-2P 379235-17-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (benzodioxolyl)pyrazinopyridoindolediones with cGMP-specific phosphodiesterase inhibiting activity useful in treating cardiovascular, erectile, and female sexual arousal disorders)

RN 379234-74-9 CAPLUS

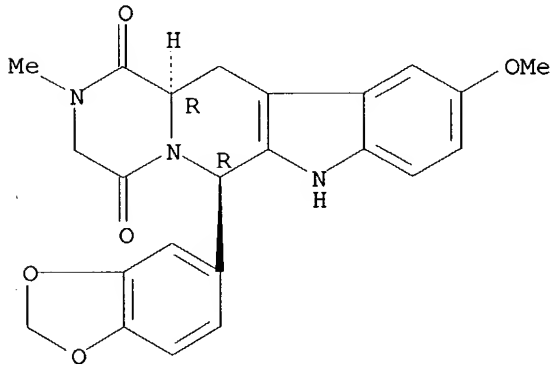
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-10-hydroxy-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



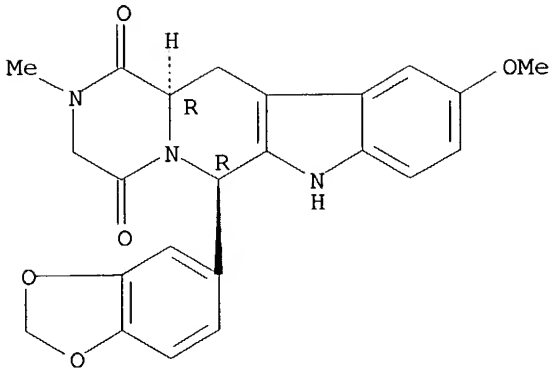
RN 379234-78-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-10-methoxy-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



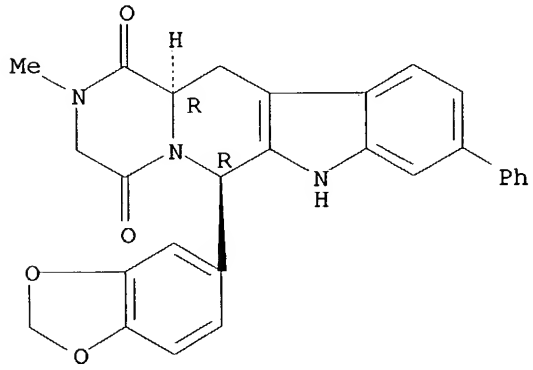
RN 379234-82-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-10-methoxy-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



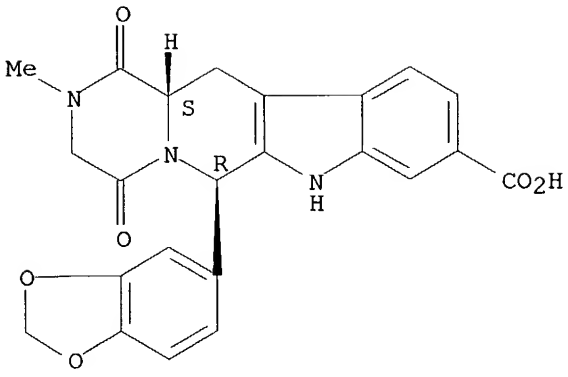
RN 379234-88-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-9-phenyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



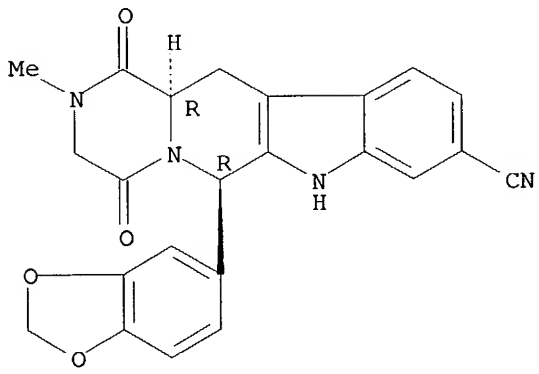
RN 379234-98-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-9-carboxylic acid, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxo-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



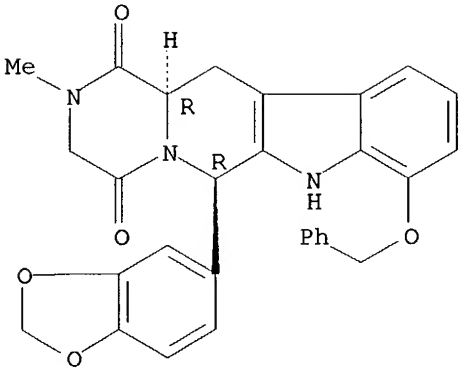
RN 379235-06-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-9-carbonitrile, 6-(1,3-benzodioxol-5-yl)-1,2,3,4,6,7,12,12a-octahydro-2-methyl-1,4-dioxo-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



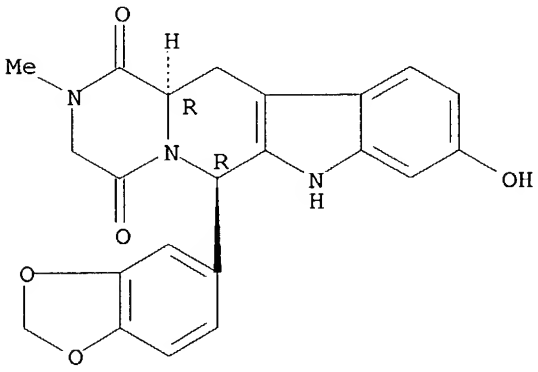
RN 379235-11-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-8-(phenylmethoxy)-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



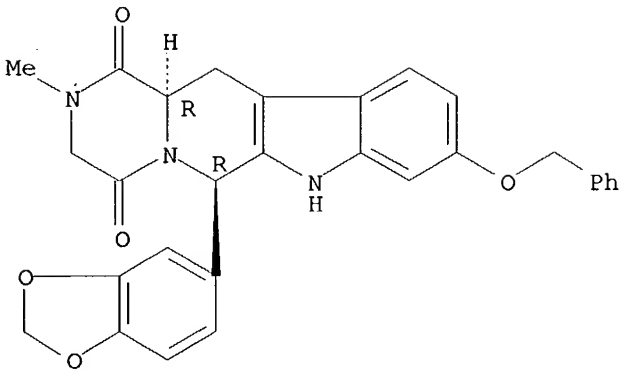
RN 379235-12-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-9-hydroxy-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



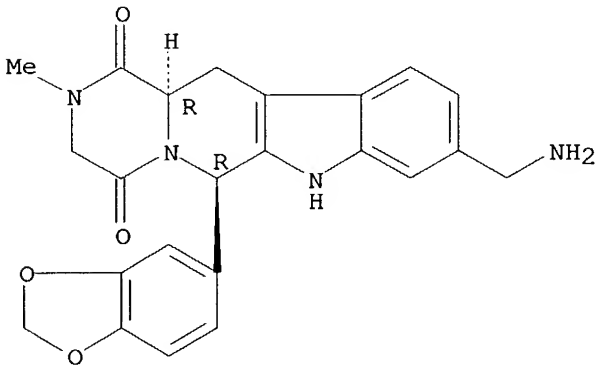
RN 379235-13-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-9-(phenylmethoxy)-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



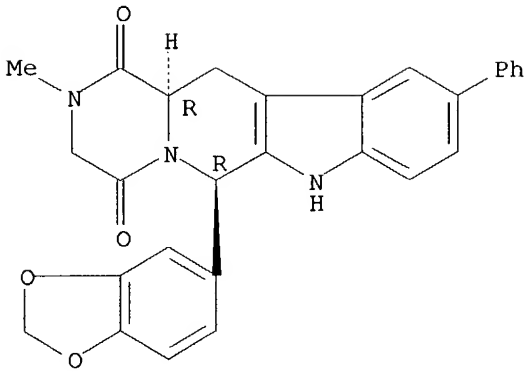
RN 379235-15-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 9-(aminomethyl)-6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



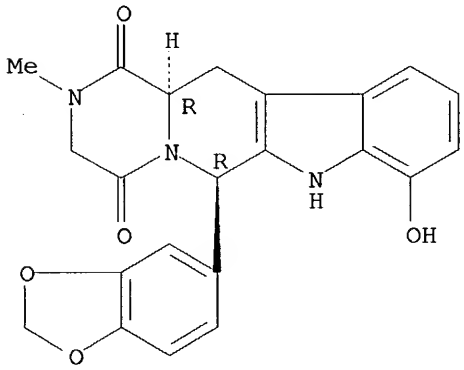
RN 379235-16-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-10-phenyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



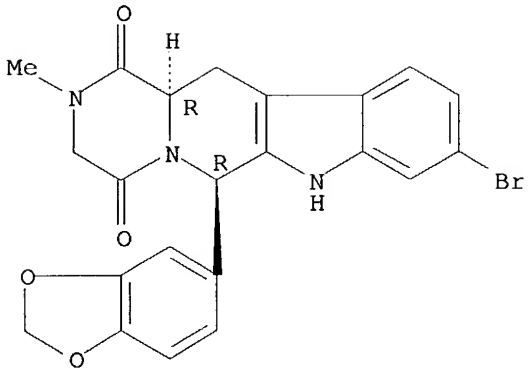
RN 379235-17-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-8-hydroxy-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **379234-87-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of (benzodioxolyl)pyrazinopyridoindolediones with cGMP-specific phosphodiesterase inhibiting activity useful in treating cardiovascular, erectile, and female sexual arousal disorders)
RN 379234-87-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-9-bromo-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.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L5 ANSWER 57 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:798055 CAPLUS
DN 135:339295
TI Daily treatment for erectile dysfunction using a phosphodiesterase 5 (PDE5) inhibitor
IN Whitaker, John S.; Saenz de Tejada, Inigo; Ferguson, Kenneth M.
PA Lilly Icos LLC, USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

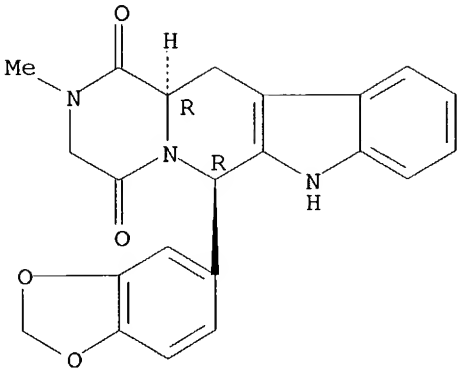
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001080860	A2	20011101	WO 2001-US12512	20010413
	WO 2001080860	A3	20020606		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6451807	B1	20020917	US 2000-558911	20000426
	EP 1276481	A2	20030122	EP 2001-927133	20010413
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001010373	A	20030218	BR 2001-10373	20010413
	JP 2003531174	T2	20031021	JP 2001-577959	20010413
	NO 2002005138	A	20021216	NO 2002-5138	20021025
PRAI	US 2000-558911	A	20000426		
	US 1999-132036P	P	19990430		
	WO 2001-US12512	W	20010413		

AB The invention relates to phosphodiesterase (PDE) enzyme inhibitors and to their use in pharmaceutical articles of manuf. In particular, the invention relates to potent inhibitors of cyclic guanosine 3',5'-monophosphate-specific phosphodiesterase type 5 (PDE5) that, when incorporated into a pharmaceutical product at about 1 to about 10 mg unit dosage, are useful for the treatment of sexual dysfunction by daily administration of the PDE5 inhibitor. The articles of manuf. are characterized by PDE5 inhibition, and accordingly provide a benefit in therapeutic areas where inhibition of PDE5 is desired, esp. erectile dysfunction, with minimization or elimination of adverse side effects resulting from inhibition of other phosphodiesterase enzymes and with an improvement of vascular conditioning.

IT **171596-29-5 171596-40-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 5 inhibitor for daily treatment for sexual dysfunction)

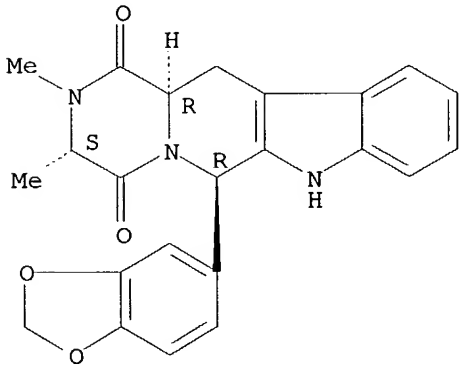
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

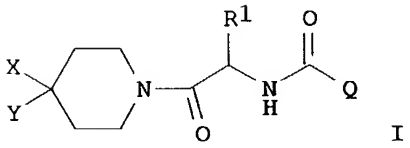
Absolute stereochemistry. Rotation (+).



L5 ANSWER 58 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:713326 CAPLUS
DN 135:272990
TI Preparation of piperazinylcarbonylaminomethylcarbonylpiperidines as melanocortin-4 receptor agonists
IN Palucki, Brenda L.; Barakat, Khaled J.; Guo, Liangqin; Lai, Yingjie; Nargund, Ravi P.; Park, Min K.; Pollard, Patrick G.; Sebhat, Iyassu K.; Ye, Zhixiong
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001070708	A1	20010927	WO 2001-US8935	20010320
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002019523	A1	20020214	US 2001-812965	20010320
	US 6458790	B2	20021001		
	EP 1268449	A1	20030102	EP 2001-922501	20010320
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003528088	T2	20030924	JP 2001-568918	20010320
PRAI	US 2000-191442P	P	20000323		
	US 2000-242265P	P	20001020		
	WO 2001-US8935	W	20010320		

OS MARPAT 135:272990
GI



I

AB Title compds. [I; Q = (substituted) (fused) piperazinyl, morpholinyl, thiomorpholinyl; R1 = H, alkyl, (substituted) cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), etc.; X = (substituted) alkyl, cycloalkyl(alkyl), aryl(alkyl), heteroaryl(alkyl), heterocyclyl(alkyl), cyano(alkyl), aminosulfonyl(alkyl), etc.; Y = H, alkyl, cycloalkyl(alkyl), (substituted) aryl(alkyl), heterocyclyl(alkyl), heteroaryl(alkyl)], were prepd. as melanocortin-4 receptor (MC-4R) agonists. Thus, capsule formulations contg. title compd. (II) were prepd. Representative I activated MC-4R with IC50<1 .mu.M. I are claimed for the treatment of

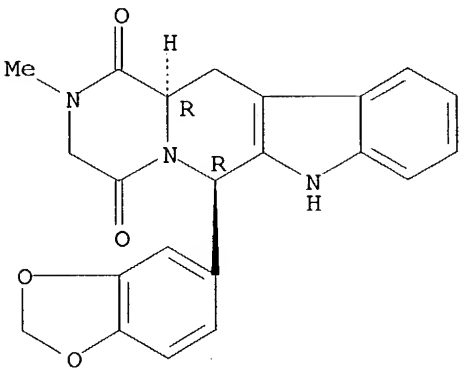
obesity, diabetes, and sexual dysfunction including erectile dysfunction and female sexual dysfunction.

IT **171596-29-5**, IC-351
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; prepn. of piperazinylcarbonylaminomethylcarbonylpiperidines as melanocortin-4 receptor agonists)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

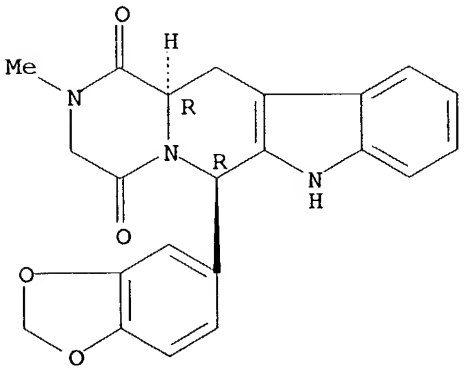
L5 ANSWER 59 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:559496 CAPLUS
DN 135:117266
TI Treatment of sexual function disorders with phosphodiesterase 4 inhibitors as monotherapy or in combination with other phosphodiesterase inhibitors or adenylate cyclase activators
PA Stief, Christian, Germany
SO Ger. Offen., 4 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 10004289	A1	20010802	DE 2000-10004289	20000201
PRAI DE 2000-10004289		20000201		

AB The invention provides a medicament contg. a phosphodiesterase 4 inhibitor as monotherapy or in combination with other phosphodiesterase inhibitors or adenylate cyclase activators for the treatment of s sexual function disorders.

IT **171596-29-5**, IC 351
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 inhibitors as monotherapy or in combination with other phosphodiesterase inhibitors or adenylate cyclase activators for treatment of sexual function disorders)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



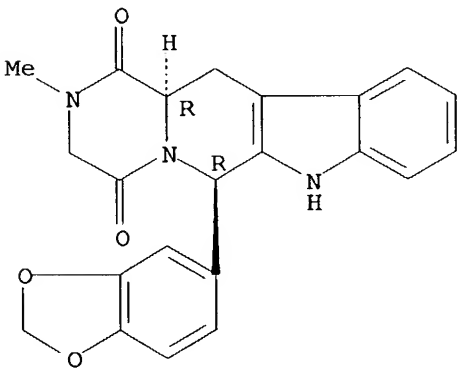
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 60 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:541505 CAPLUS
DN 135:132460
TI Treatment of sexual function disorders with guanylate cyclase activators, optionally in combination with phosphodiesterase inhibitors
IN Stief, Christian; Magerl, Hans-Jurgen; Kuthe, Andrea; Uckert, Stefan; Becker, Armin; Farssmann, Wolf Georg; Jones, Udo
PA Germany
SO Ger. Offen., 6 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 10002200	A1	20010726	DE 2000-10002200	20000119
PRAI DE 2000-10002200		20000119		

AB Medicaments contg. activators of guanylate cyclase and their variants, individually or in combination with phosphodiesterase inhibitors, are provided for the treatment of sexual function disorders. e.g. erectile dysfunction.
IT **171596-29-5**, IC 351
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(guanylate cyclase activators, optionally in combination with phosphodiesterase inhibitors, for treatment of sexual function disorders)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 61 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:338071 CAPLUS
DN 134:336223
TI Treatment of pulmonary hypertension with sildenafil or other phosphodiesterase V inhibitor
IN Butrous, Ghazwan Saleem; Lukas, Timothy; Machin, Ian
PA Pfizer Limited, UK; Pfizer Inc.
SO Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

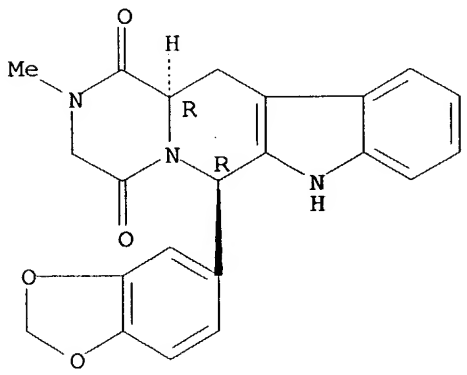
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1097711	A2	20010509	EP 2000-309212	20001101
	EP 1097711	A3	20010801		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	ZA 2000006165	A	20020430	ZA 2000-6165	20001031
	JP 2001172182	A2	20010626	JP 2000-335765	20001102
PRAI	GB 1999-25970	A	19991102		
	GB 2000-3235	A	20000211		

AB This invention relates to the use of certain cyclic guanosine 3',5'-monophosphate phosphodiesterase type 5 inhibitors, including in particular the compd. sildenafil, for the treatment of pulmonary hypertension.

IT **171596-29-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sildenafil or other phosphodiesterase V inhibitor for treatment of pulmonary hypertension)

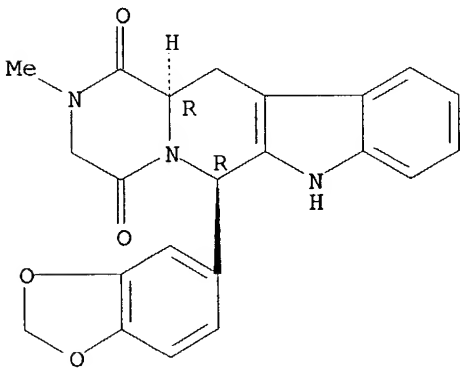
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 62 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:258390 CAPLUS
DN 135:189567
TI IC-351: Treatment of erectile dysfunction treatment of female sexual dysfunction phosphodiesterase 5 inhibitor
AU Sorbera, L. A.; Martin, L.; Leeson, P. A.; Castaner, J.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (2001), 26(1), 15-19
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
AB A review with 20 refs. Significantly more patients (86 %) given IC-351 reported enhanced erections as compared to placebo and a significant change in the patient's median rating was obsd. with IC-351 treatment as compared to placebo. IC-351 (ClalisTM) continues to undergo phase III trials as a treatment for male erectile dysfunction and phase II trials as a treatment for female sexual dysfunction.
IT **171596-29-5**, IC 351
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IC-351 in treatment of erectile dysfunction and treatment of female sexual dysfunction in humans)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 63 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:100983 CAPLUS
DN 134:152655
TI Pharmaceutical compositions containing .beta.-carboline drugs
IN Anderson, Neil R.; Hartauer, Kerry J.; Kral, Martha A.; Stephenson, Gregory A.
PA Lilly Icos Llc, USA
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2

APPS

DT Patent
LA English
FAN.CNT 1

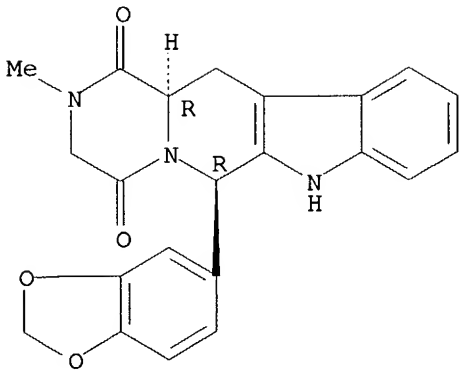
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001008688	A2	20010208	WO 2000-US20981	20000801
	WO 2001008688	A3	20010816		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 2000012901	A	20020416	BR 2000-12901	20000801
	EP 1200092	A2	20020502	EP 2000-952371	20000801
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003505510	T2	20030212	JP 2001-513418	20000801
	NZ 516613	A	20030829	NZ 2000-516613	20000801
	ZA 2002000825	A	20030207	ZA 2002-825	20020130
	NO 2002000531	A	20020403	NO 2002-531	20020201
PRAI	US 1999-147048P	P	19990803		
	WO 2000-US20981	W	20000801		

AB Pharmaceutical compns. contg. .beta.-carboline drugs and pharmaceutically acceptable salts and solvates thereof, wherein the drug is in free particulate form, is disclosed. A tablet contained a .beta.-carboline drug 10.00, lactose monohydrate 153.80, spray dried lactose monohydrate 25.00, hydroxypropyl cellulose 4.00, croscarmellose sodium 16.00, hydroxypropyl cellulose 1.75, sodium lauryl sulfate 0.70, microcryst. cellulose 37.50, and magnesium stearate 1.25 mg. The improvement in bioavailability of the drug was demonstrated in humans.

IT **171596-29-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. .beta.-carboline drugs)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).


O
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L5 ANSWER 64 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:100982 CAPLUS
DN 134:152654
TI .beta.-Carboline pharmaceutical compositions
IN Anderson, Neil R.; Gullapalli, Rampurna P.
PA Lilly Icos Llc, USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

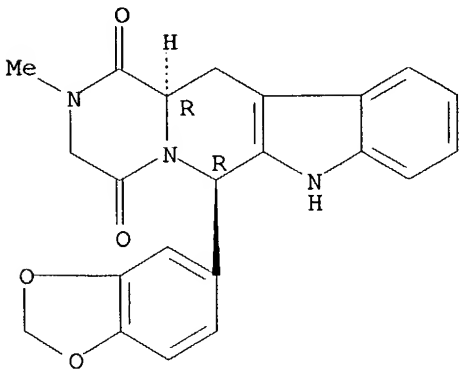
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001008687	A1	20010208	WO 2000-US11136	20000426
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1200091	A1	20020502	EP 2000-926371	20000426
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	ZA 2002000823	A	20030204	ZA 2002-823	20020130
PRAI	US 1999-146924P	P	19990803		
	WO 2000-US11136	W	20000426		

AB .beta.-Carboline soft capsules contains a soln. or suspension of a PDE5 inhibitor, and are useful for treating sexual dysfunction. Thus, a formulation contained a .beta.-carboline 25.0, Capmul MCM 177.5, Gelucire 44/14 177.5, and propylene glycol 20.0 mg/capsule. In the phys. study of the above capsule formulation, no sedimentation was obsd. after storage at 4.degree. for 120 days.

IT **171596-29-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-carboline pharmaceutical compns.)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 65 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:100981 CAPLUS
DN 134:152653
TI .beta.-Carboline pharmaceutical compositions containing cellulose
IN Oren, Peter L.; Anderson, Neil R.; Kral, Martha A.
PA Lilly Icos Llc, USA
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

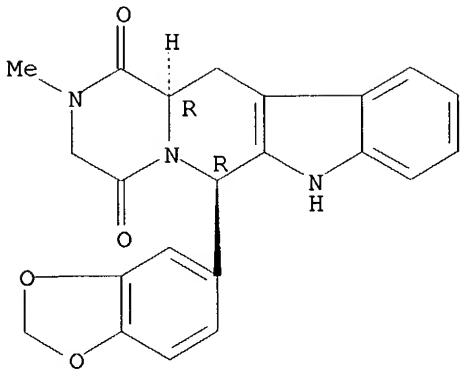
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001008686	A1	20010208	WO 2000-US11130	20000426
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	BR 2000012863	A	20020416	BR 2000-12863	20000426
	EP 1200090	A1	20020502	EP 2000-926368	20000426
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003505509	T2	20030212	JP 2001-513416	20000426
	NZ 516616	A	20030725	NZ 2000-516616	20000426
	ZA 2002000823	A	20030204	ZA 2002-823	20020130
	NO 2002000532	A	20020326	NO 2002-532	20020201
PRAI	US 1999-146924P	P	19990803		
	WO 2000-US11130	W	20000426		

AB .beta.-Carboline formulations contain a c-GMP phosphodiesterase inhibitor, a water-sol. diluent, a lubricant, a hydrophilic binder, a disintegrant, and optional microcryst. cellulose and/or a wetting agent, are useful for treating sexual dysfunction. Thus, a tablet formulation contained a .beta.-carboline 5.00, lactose monohydrate 109.655, lactose monohydrate (spray dried) 17.50, Hydroxypropyl cellulose 4.025, croscarmellose sodium 6.30, SLS 0.49, microcryst. cellulose (granular-102) 26.25, croscarmellose sodium 4.90, and Mg stearate 0.88 mg/tablet.

IT **171596-29-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-carboline pharmaceutical compns. contg. cellulose)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 66 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:28490 CAPLUS
DN 134:95523
TI Drugs for the increase of the cAMP levels
IN Stief, Christian G.; Ueckert, Stefan; Becker, Armin; Jonas, Udo; Forssmann, Wolf-Georg
PA Germany
SO Ger. Offen., 6 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

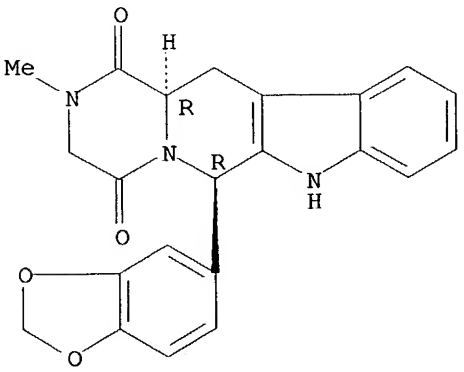
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 19931206	A1	20010111	DE 1999-19931206	19990707
PRAI DE 1999-19931206		19990707		

AB The invention concerns drugs for the increase of the cAMP levels and/or for the inhibition of the cAMP hydrolysis in smooth muscle tissues and their use for the treatment of diseases. Compds. such as sildenafil increased the cAMP levels in smooth muscle tissues.

IT **171596-29-5**, IC 351
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drugs for increase of cAMP levels)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 67 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:790302 CAPLUS
DN 133:329631
TI Treatment of female arousal disorder with a type V cGMP phosphodiesterase inhibitor
IN Allemeier, Lora L.; Brashear, Diane L.; Ferguson, Kenneth M.; Pullman, William E.
PA Lilly Icos LLC, USA
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

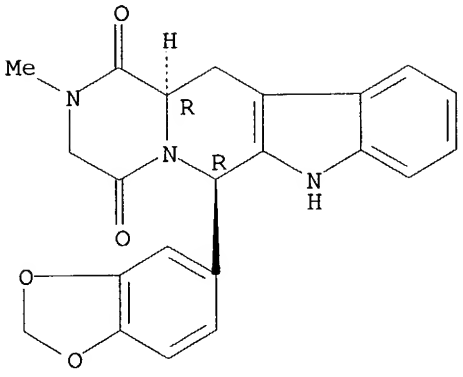
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000066114	A1	20001109	WO 2000-US11128	20000426
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1173167	A1	20020123	EP 2000-928382	20000426
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002543128	T2	20021217	JP 2000-614999	20000426
	US 6613768	B1	20030902	US 2001-31321	20011019
PRAI	US 1999-132129P	P	19990430		
	WO 2000-US11128	W	20000426		

AB A method of treating female arousal disorder in a female patient is disclosed. The method includes orally administering an agent that inhibits cyclic guanosine 3',5'-monophosphate-specific phosphodiesterase type 5 to the female patient.

IT **171596-29-5 171596-40-0 304683-09-8**
304683-11-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cGMP phosphodiesterase type V inhibitor for treatment of female arousal disorder)

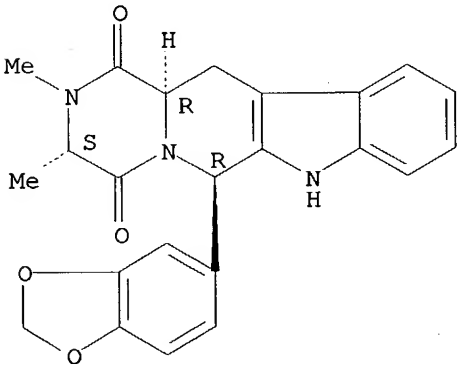
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

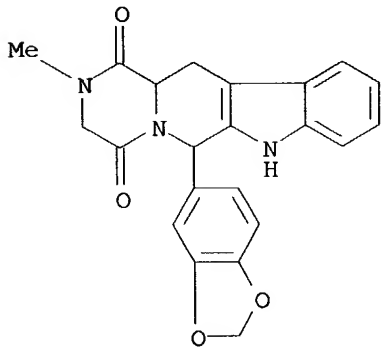


RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

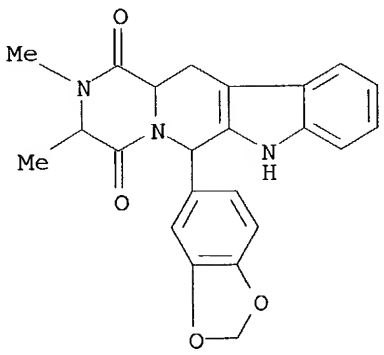


RN 304683-09-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl- (9CI) (CA INDEX NAME)



RN 304683-11-2 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl- (9CI) (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 68 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:785898 CAPLUS
DN 133:329627
TI Tetracyclic cGMP-specific phosphodiesterase inhibitors and their use in disease treatment
IN Daugan, Alain Claude Marie; Gellibert, Francoise
PA Icos Corp., USA
SO U.S., 30 pp., Cont.-in-part of PCT 9519978.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6143746	A	20001107	US 1998-154051	19980916
	WO 9519978	A1	19950727	WO 1995-EP183	19950119
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	WO 9703675	A1	19970206	WO 1996-EP3024	19960711
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
	WO 9703985	A1	19970206	WO 1996-EP3025	19960711
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	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
	US 6025494	A	20000215	US 1998-133078	19980812
	CA 2340636	AA	20000323	CA 1999-2340636	19990826
	EP 1113800	A1	20010711	EP 1999-945201	19990826
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002524516	T2	20020806	JP 2000-569812	19990826
	US 6127542	A	20001003	US 1999-399667	19990921
	US 6369059	B1	20020409	US 2000-633431	20000807
	CZ 289832	B6	20020417	CZ 2000-3428	20000919
	US 2002119976	A1	20020829	US 2002-68114	20020205
PRAI	GB 1994-1090	A	19940121		
	WO 1995-EP183	A2	19950119		
	GB 1995-14464	A	19950714		
	GB 1995-14465	A	19950714		
	WO 1996-EP3024	A2	19960711		
	WO 1996-EP3025	A2	19960711		
	CZ 1998-33	A3	19960711		
	US 1996-669389	A3	19960716		
	US 1998-133078	A1	19980812		
	US 1998-154051	A	19980916		
	WO 1999-US19466	W	19990826		

US 1999-399667 A1 19990921
US 2000-633431 A1 20000807
OS MARPAT 133:329627
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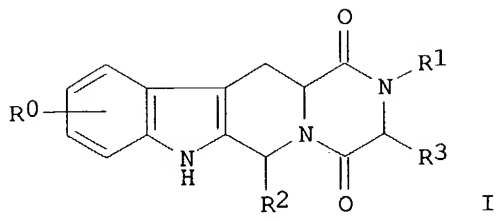


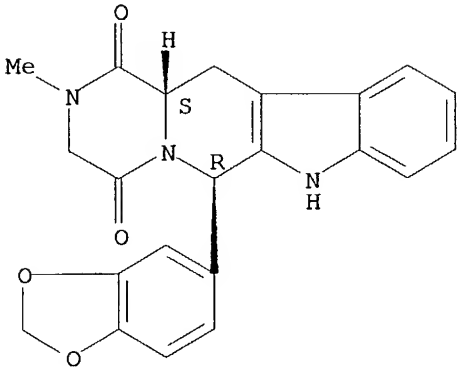
I

AB A compd. of formula I (R0 = H, halogen, C1-6 alkyl; R1 = H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, halo-C1-6 alkyl, C3-8 cycloalkyl, C3-8 cycloalkyl-C1-3 alkyl, aryl-C1-3 alkyl, heteroaryl-C1-3 alkyl; R2 = (substituted) monocyclic arom. ring selected from benzene, thiophene, furan, and pyridine, or (substituted) bicyclic ring (a) attached to the rest of the mol. via one of the benzene ring carbon atoms, and wherein the fused ring is a 5- or 6-membered ring which may be satd. or partially or fully unsatd., and comprises carbon atoms and optionally one or two heteroatoms selected from oxygen, sulfur, and nitrogen; R3 = H, C1-3 alkyl, or R1 and R3 together = 3- or 4-membered alkyl or alkenyl chain) and salts and solvates thereof is disclosed. Compd. I is a potent and selective inhibitor of cyclic guanosine 3',5'-monophosphate-specific phosphodiesterase, having a utility in a variety of therapeutic areas where such inhibition is beneficial, including the treatment of cardiovascular disorders and erectile dysfunction. Thus, many I compds. were synthesized and tested in vitro as inhibitors of cGMP phosphodiesterase. Cis-2,3,6,7,12,12a-hexahydro-2-(4-pyridylmethyl)-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione showed IC50 of 10 nM.

IT **171488-01-0P 171488-03-2P 171488-04-3P**
171488-06-5P 171488-07-6P 171488-08-7P
171488-09-8P 171488-10-1P 171488-11-2P
171488-12-3P 171488-13-4P 171488-14-5P
171488-15-6P 171488-16-7P 171488-17-8P
171488-18-9P 171488-19-0P 171488-20-3P
171488-21-4P 171488-22-5P 171488-76-9P
171488-77-0P 171488-86-1P 171488-87-2P
171488-91-8P 171488-92-9P 171488-94-1P
171488-95-2P 171489-02-4P 171596-27-3P
171596-28-4P 171596-29-5P 171596-30-8P
171596-31-9P 171596-32-0P 171596-36-4P
171596-40-0P 187935-15-5P 303984-32-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tetracyclic cyclic GMP-specific phosphodiesterase inhibitors and their use in disease treatment)

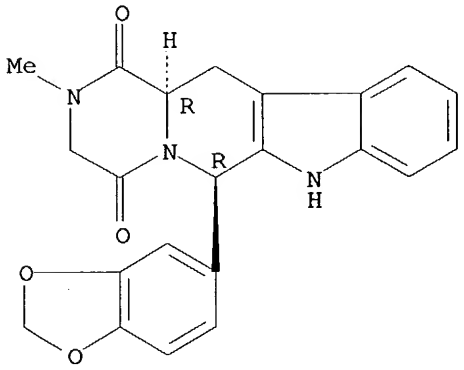
RN 171488-01-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



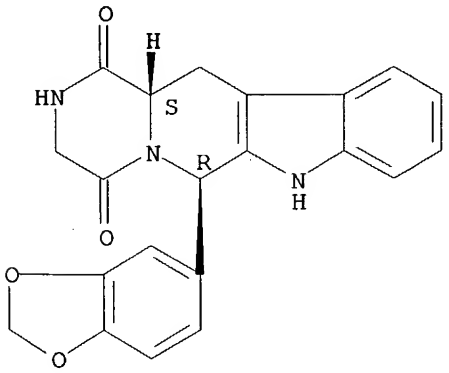
RN 171488-03-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



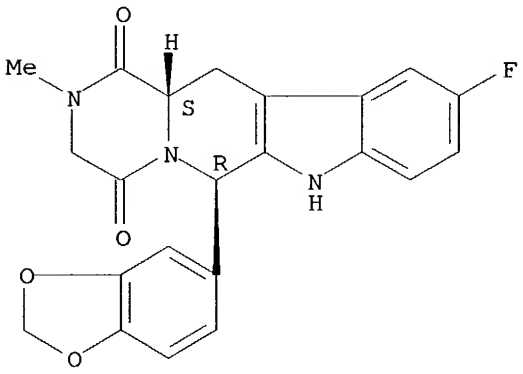
RN 171488-04-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



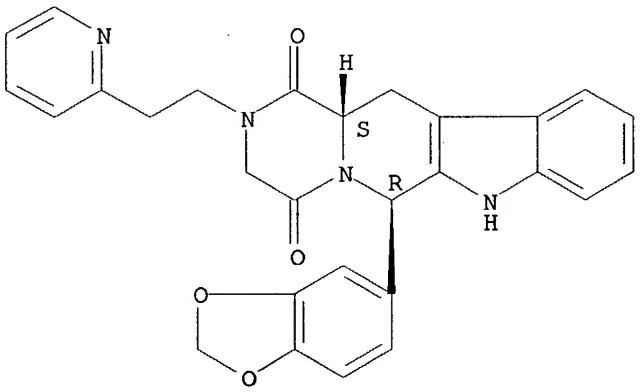
RN 171488-06-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-10-fluoro-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



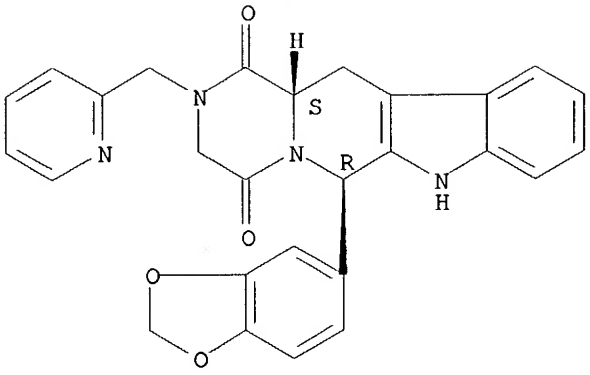
RN 171488-07-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(2-pyridinyl)ethyl]-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



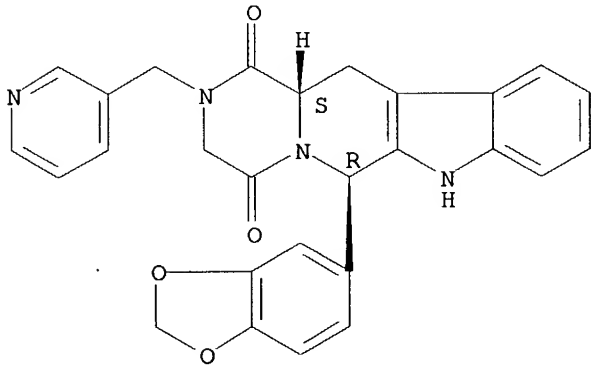
RN 171488-08-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



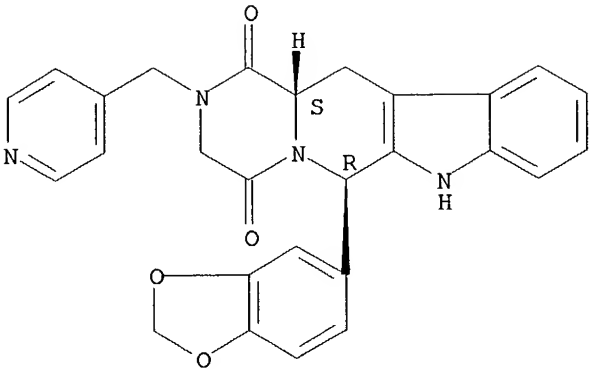
RN 171488-09-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(3-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



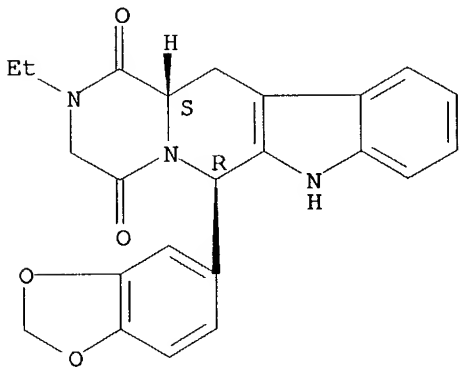
RN 171488-10-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(4-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



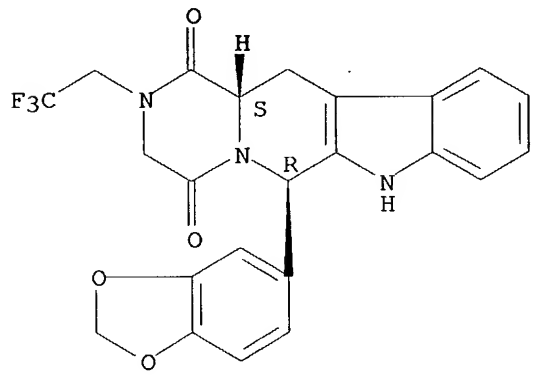
RN 171488-11-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-ethyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



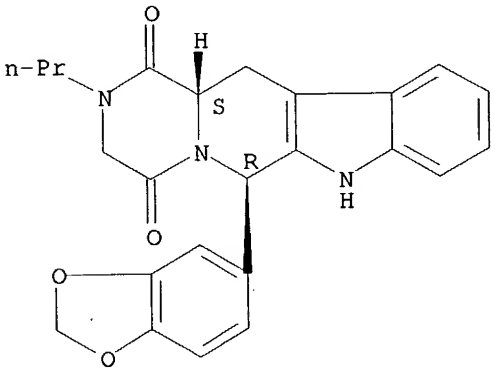
RN 171488-12-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2,2,2-trifluoroethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



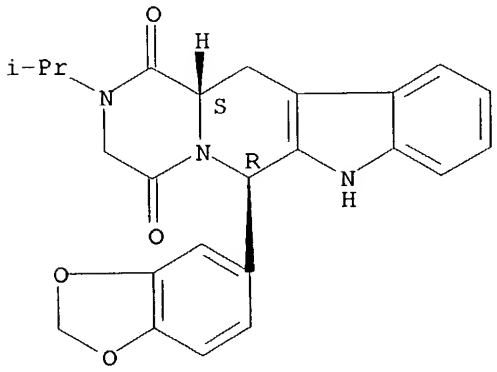
RN 171488-13-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-propyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



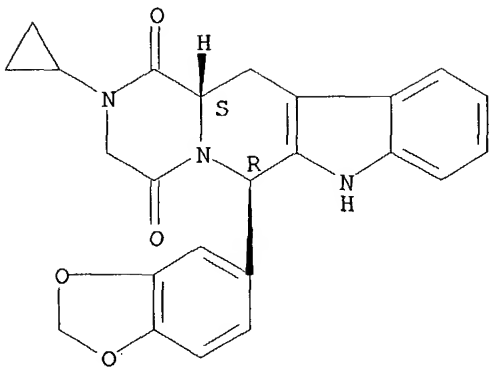
RN 171488-14-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(1-methylethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



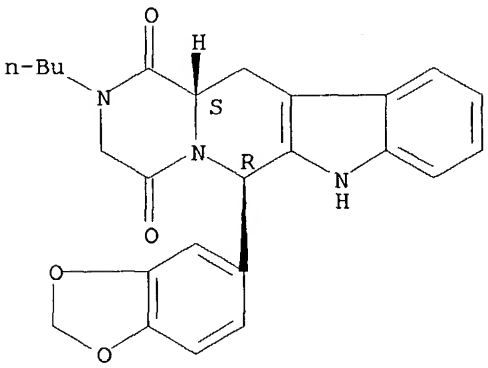
RN 171488-15-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopropyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



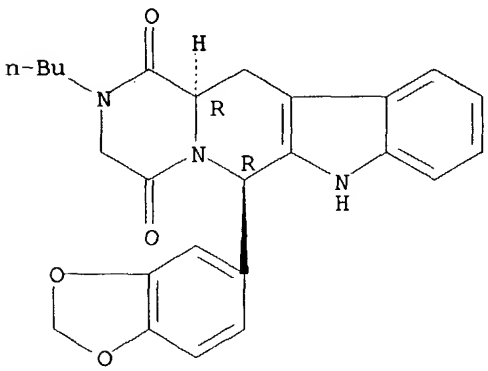
RN 171488-16-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



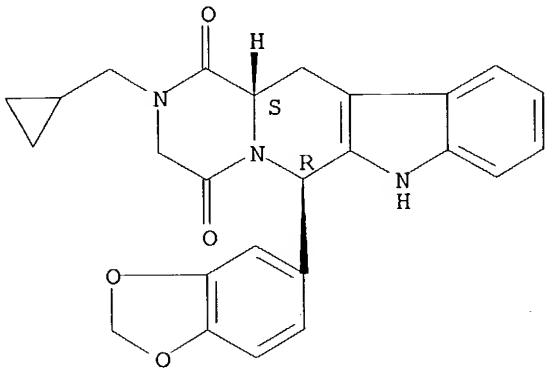
RN 171488-17-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



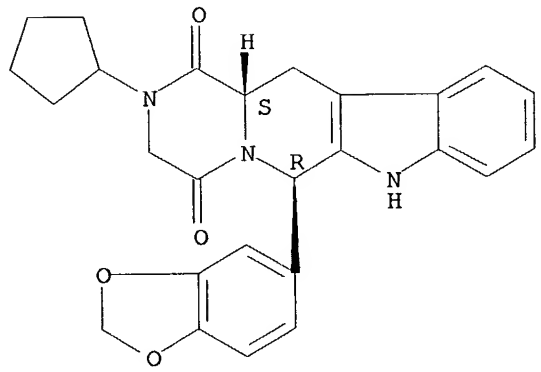
RN 171488-18-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(cyclopropylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



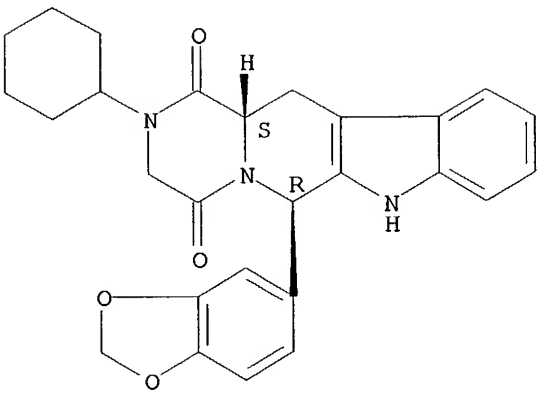
RN 171488-19-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopentyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



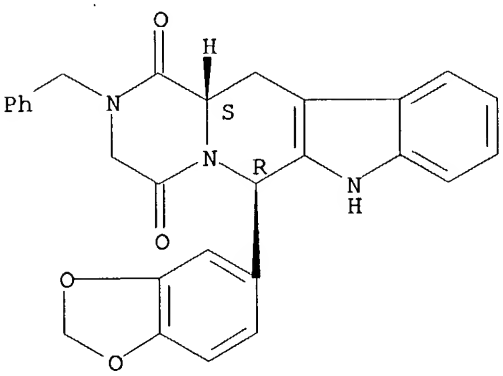
RN 171488-20-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclohexyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



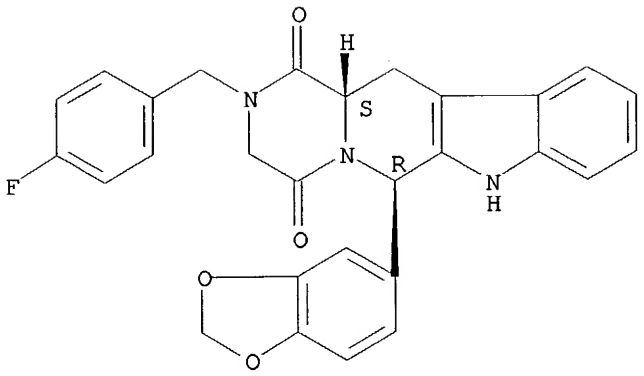
RN 171488-21-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(phenylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



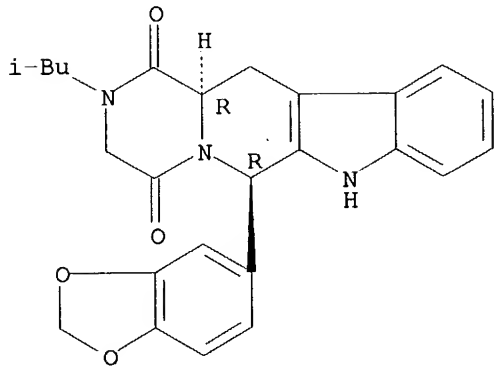
RN 171488-22-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[(4-fluorophenyl)methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



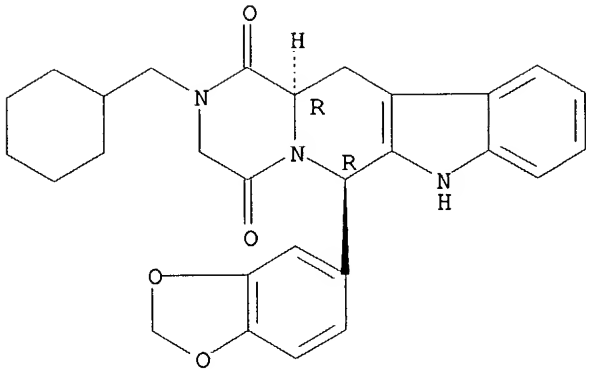
RN 171488-76-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-methylpropyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



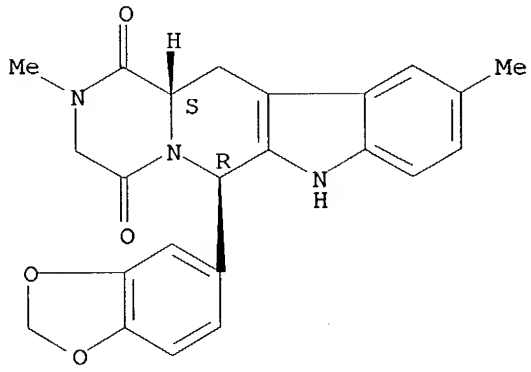
RN 171488-77-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(cyclohexylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



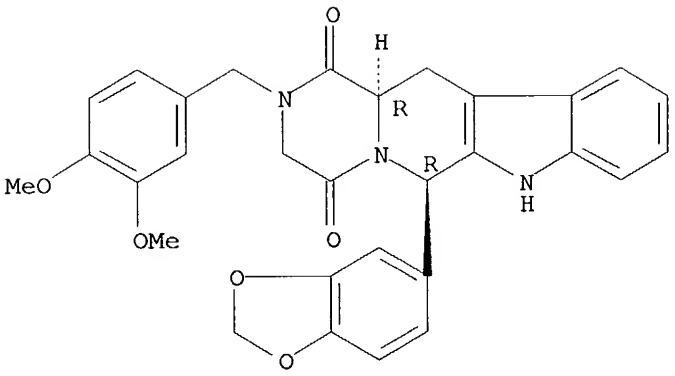
RN 171488-86-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,10-dimethyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



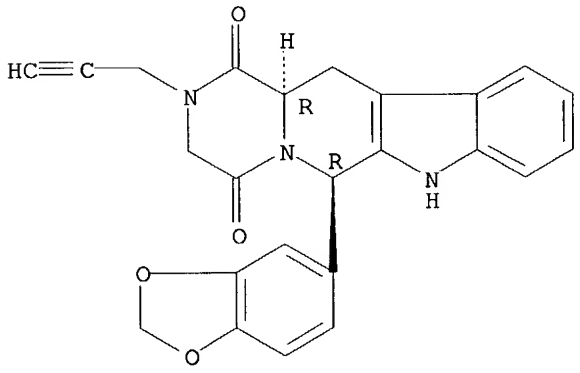
RN 171488-87-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[(3,4-dimethoxyphenyl)methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



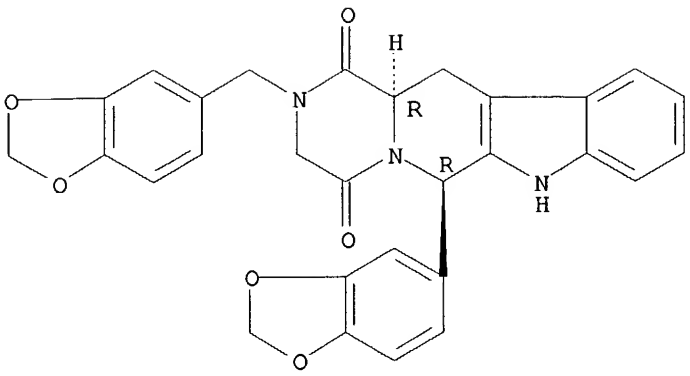
RN 171488-91-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-propynyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



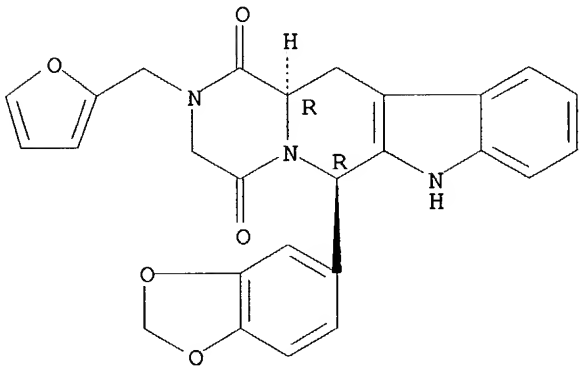
RN 171488-92-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(1,3-benzodioxol-5-ylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



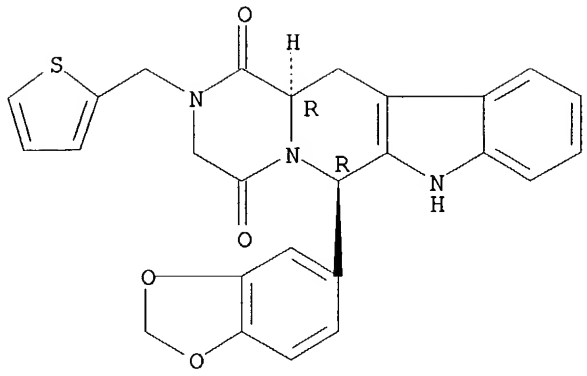
RN 171488-94-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(2-furanylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



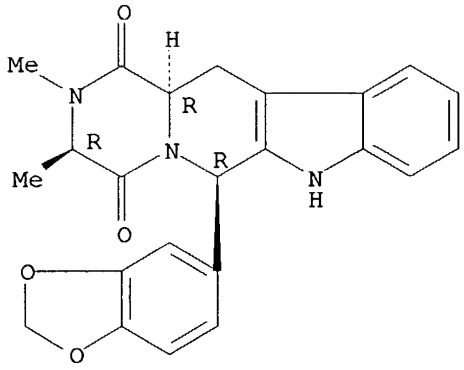
RN 171488-95-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-thienylmethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



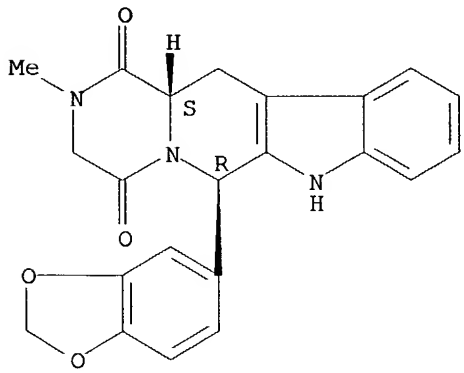
RN 171489-02-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3R,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



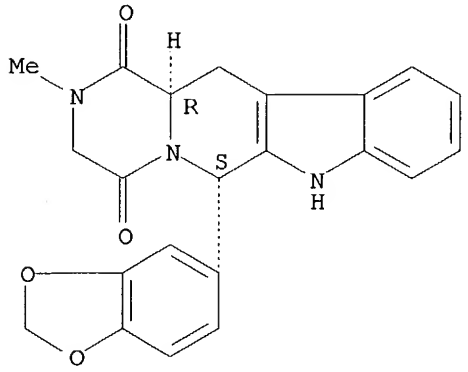
RN 171596-27-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



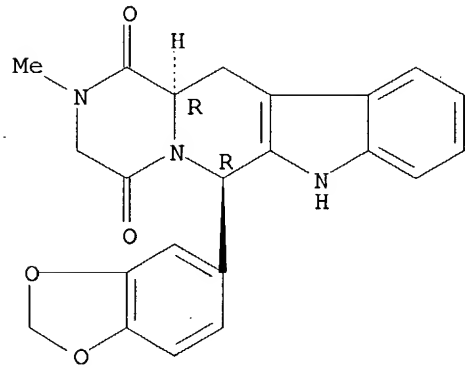
RN 171596-28-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6S,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



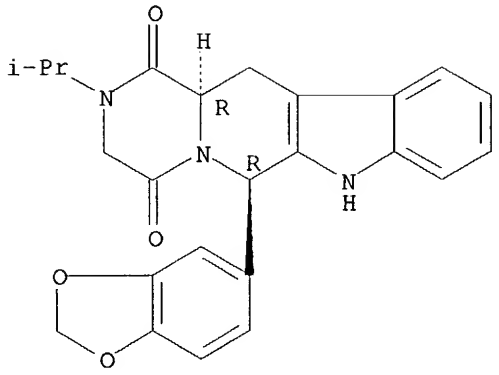
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



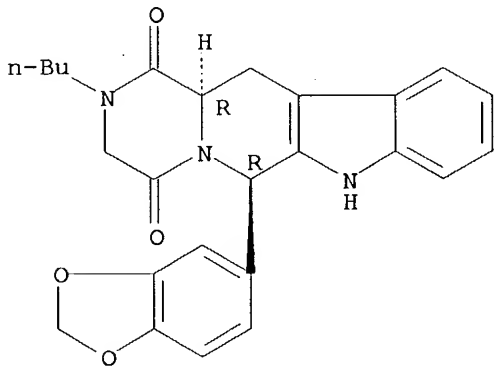
RN 171596-30-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(1-methylethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



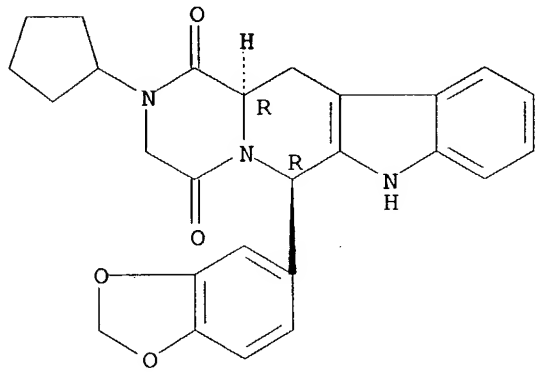
RN 171596-31-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



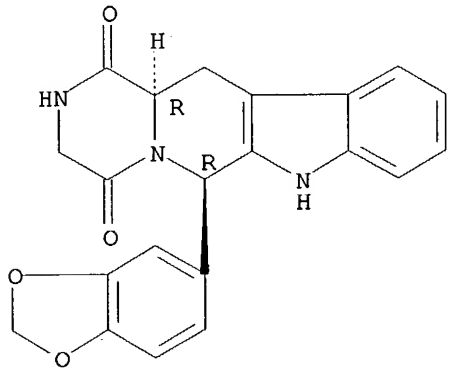
RN 171596-32-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopentyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



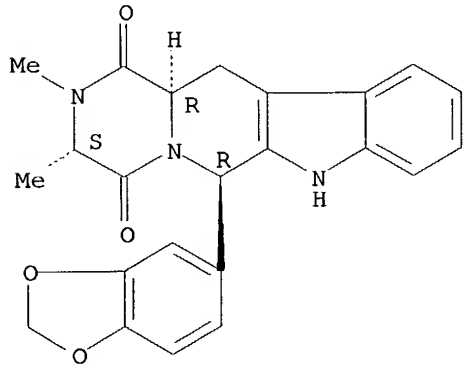
RN 171596-36-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



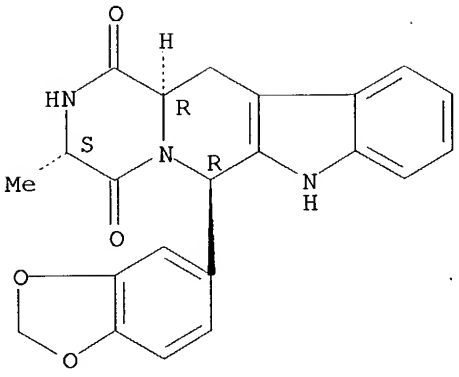
RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



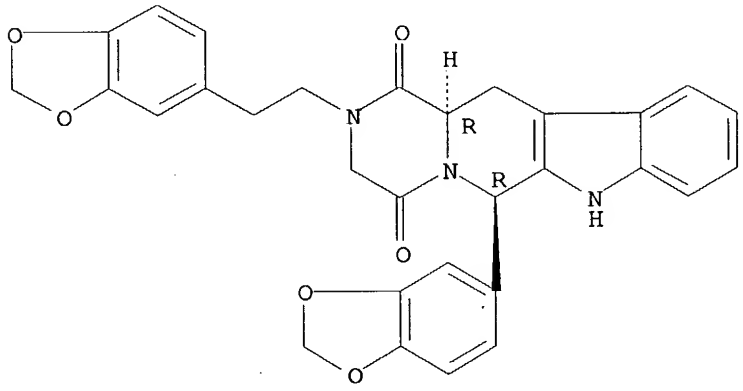
RN 187935-15-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-methyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 303984-32-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-(1,3-benzodioxol-5-yl)ethyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 69 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:686171 CAPLUS
DN 133:271672
TI Phosphodiesterase inhibitor preparation for treatment of sexual functional disorders
PA Lilly Icos Llc, USA
SO Ger. Gebrauchsmusterschrift, 47 pp.
CODEN: GGXXFR
DT Patent
LA German
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 20007861	U1	20000928	DE 2000-20007861	20000426
	NO 2000002097	A	20011026	NO 2000-2097	20000425
	ES 2187234	A1	20030516	ES 2000-1055	20000425
	CA 2307101	AA	20001030	CA 2000-2307101	20000426
	CA 2307101	C	20030128		
	FI 2000000976	A	20001030	FI 2000-976	20000426
	NL 1015027	A1	20001031	NL 2000-1015027	20000426
	NL 1015027	C2	20010214		
	SE 2000001518	A	20001031	SE 2000-1518	20000426
	ZA 2000002058	A	20001102	ZA 2000-2058	20000426
	WO 2000066099	A2	20001109	WO 2000-US11129	20000426
	WO 2000066099	A3	20010118		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 10021266	A1	20001116	DE 2000-10021266	20000426
	PT 102457	A	20001130	PT 2000-102457	20000426
	JP 2000336043	A2	20001205	JP 2000-126472	20000426
	FR 2795646	A1	20010105	FR 2000-5296	20000426
	FR 2795646	B1	20020816		
	GB 2351663	A1	20010110	GB 2000-10199	20000426
	LT 4758	B	20010226	LT 2000-35	20000426
	LV 12560	B	20010420	LV 2000-56	20000426
	CN 1292264	A	20010425	CN 2000-106987	20000426
	SI 20361	C	20010430	SI 2000-107	20000426
	BE 1012957	A5	20010605	BE 2000-295	20000426
	NZ 504163	A	20011130	NZ 2000-504163	20000426
	HR 2000000243	A1	20011231	HR 2000-243	20000426
	EP 1173181	A2	20020123	EP 2000-926367	20000426
	EP 1173181	B1	20031015		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	LU 90569	A2	20020227	LU 2000-90569	20000426
	CH 692478	A	20020715	CH 2000-81900	20000426
	BR 2000003046	A	20020723	BR 2000-3046	20000426
	JP 2002543116	T2	20021217	JP 2000-614984	20000426
	BR 2000010181	A	20030225	BR 2000-10181	20000426
	NZ 514882	A	20030829	NZ 2000-514882	20000426
	AT 251908	E	20031115	AT 2000-926367	20000426

	HR 2001000778	A1	20021231	HR 2001-778	20011023
	NO 2001005275	A	20011206	NO 2001-5275	20011029
PRAI	US 1999-132036P	P	19990430		
	WO 2000-US11129	W	20000426		

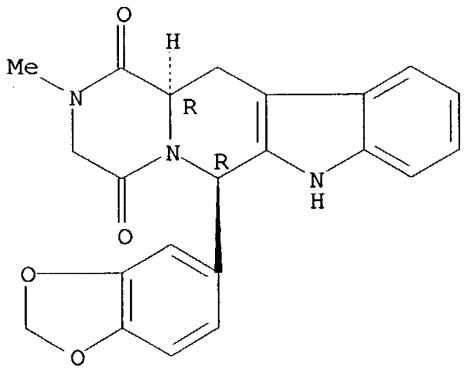
AB A formulation for the treatment of sexual malfunctions (e.g., erectile dysfunction in men and decreased libido in women) which contains a phosphodiesterase 5 inhibitor with a IC50 of at least 100-fold lower than that with phosphodiesterase 6 as active ingredient, and which inhibits phosphodiesterase 5 with an IC50 of at least 1000-fold lower than for phosphodiesterase 1c and a IC50 for PDE5 of below 10 nM.

IT **171596-29-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(phosphodiesterase inhibitor prepn. for treatment of sexual functional disorders)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



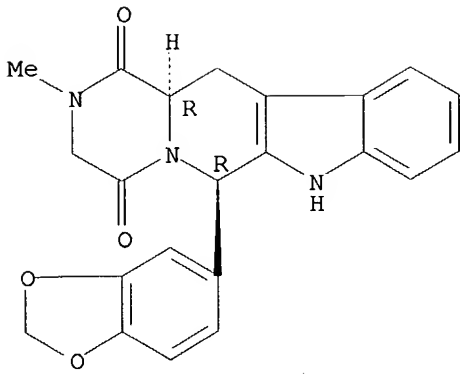
L5 ANSWER 70 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:666601 CAPLUS
DN 133:256811
TI Pharmaceutical compositions containing dopamine agonists in combination with nitric oxide donors for treating and/or preventing sexual dysfunctions
IN Garvey, David S.
PA Nitromed, Inc., USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000054773	A1	20000921	WO 2000-US3709	20000310

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-123920P P 19990312
OS MARPAT 133:256811
AB The present invention is directed to novel compns. comprising at least one dopamine agonist in combination with at least one nitric oxide donor (i.e. compds. that donate, transfer or release nitric oxide, elevate endogenous levels of endothelium-derived relaxing factor, stimulate endogenous synthesis of nitric oxide or are substrates for nitric oxide synthase). The novel compns. may optionally comprise at least one therapeutic agent, such as, a vasoactive agent, an antiemetic agent, and mixts. thereof. The dopamine agonist is preferably apomorphine. The present invention is also directed to methods for treating and/or preventing sexual dysfunctions and/or enhancing sexual responses in patients. In other embodiments, the present invention is directed to methods treating or preventing neurodegenerative diseases, mitochondrial diseases, spinal cord injury, central or psychostimulant addiction, senile dementia, circulatory disorders, cardiovascular disorders, hyperprolactinemia or myopia. The compds. and/or compns. of the present invention can also be provided in the form of a pharmaceutical kit (no data).
IT **171596-29-5**, Ic 351
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. dopamine agonists in combination with nitric oxide donors for treating and/or preventing sexual dysfunctions)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



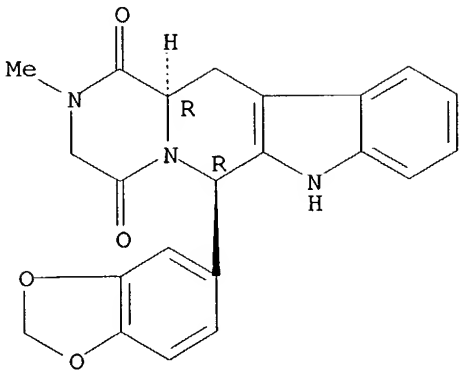
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 71 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:645819 CAPLUS
DN 133:227820
TI Pharmaceutical compositions for treating erectile dysfunction containing a melanocortin receptor agonist and a cyclic-GMP-specific phosphodiesterase inhibitor or an .alpha.-adrenergic receptor antagonist
IN Stoner, Elizabeth
PA Merck & Co., Inc., USA; Waldstreicher, Joanne
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000053148	A2	20000914	WO 2000-US5711	20000303
	WO 2000053148	A3	20001214		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1161255	A2	20011212	EP 2000-916081	20000303
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1999-123244P	P	19990308		
	WO 2000-US5711	W	20000303		

AB The present invention provides for a method for the treatment of erectile dysfunction in a male or female human subject in need of such treatment comprising administration of a therapeutically effective amt. of an agonist of the melanocortin receptor in combination with a therapeutically effective amt. of a cyclic-GMP-specific phosphodiesterase inhibitor or an alpha-adrenergic receptor antagonist. Further, the present invention provides for pharmaceutical compns. useful in the methods of the present invention, as well as a method of manuf. of a medicament useful for treating erectile dysfunction. Effect of the combination of 20 mg/kg of the invention compds. was tested in rats. A hard gelatin capsule contained a melanocortin receptor agonist 5, and a type V phosphodiesterase inhibitor 10 mg.
IT **171596-29-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. for treating erectile dysfunction contg. melanocortin receptor agonist and cyclic-GMP-specific phosphodiesterase inhibitor or .alpha.-adrenergic receptor antagonist)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).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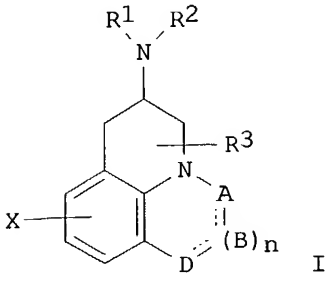
L5 ANSWER 72 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:475525 CAPLUS
DN 133:109946
TI Methylaminodihydroimidazoquinolinones for treating sexual disturbances and inducing mating in animals
IN Meglasson, Martin Durham; McCall, Robert B.
PA Pharmacia & Upjohn Company, USA
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000040226	A2	20000713	WO 1999-US27951	19991220
	WO 2000040226	A3	20010201		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6455564	B1	20020924	US 1999-465668	19991217
	BR 9916759	A	20010925	BR 1999-16759	19991220
	EP 1140092	A2	20011010	EP 1999-967142	19991220
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002534376	T2	20021015	JP 2000-591983	19991220
	NZ 512820	A	20021220	NZ 1999-512820	19991220
	ZA 2001004283	A	20020524	ZA 2001-4283	20010524
	US 2002107247	A1	20020808	US 2002-78611	20020219
	US 2002198187	A1	20021226	US 2002-208353	20020730
	US 2003004152	A1	20030102	US 2002-208084	20020730
	US 2003013710	A1	20030116	US 2002-208644	20020730
PRAI	US 1999-114840P	P	19990106		
	US 1999-115051P	P	19990108		
	US 1999-115922P	P	19990114		
	US 1999-120543P	P	19990217		
	US 1999-465668	A3	19991217		
	WO 1999-US27951	W	19991220		
	US 2002-78611	A3	20020219		

OS MARPAT 133:109946
GI



I

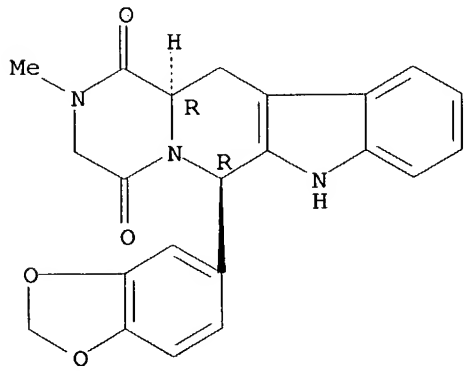
AB The present invention is a method of treating sexual disturbances in humans and inducing mating in non-human mammals using the compds. of formula (I: R1,R2,R3 = H, alkyl, alkenyl, cycloalkyl, etc.; X = H, alkyl, halogen, OH, etc.; A,B,D = CH, CH2, CO, N, etc.; n = 0 or 1) in a dosage range where the sexually therapeutic amt. is from about 0.2 through 8 mg/person/dose and where the sexually mating amt. is from about 0.003 through 0.2 mg/kg/dose.

IT **171596-29-5,** ICOS 351
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(treating sexual disturbances and inducing mating in animals)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

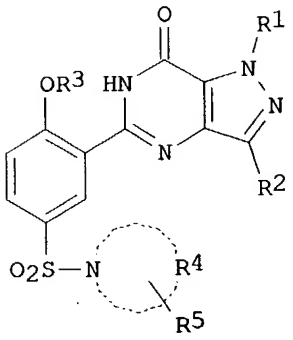
Absolute stereochemistry. Rotation (+).



L5 ANSWER 73 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:392967 CAPLUS
DN 133:22405
TI Preventives containing 1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one derivatives and related compounds for nitric acid-induced tolerance
IN Ellis, Peter
PA Pfizer Inc., USA
SO Jpn. Kokai Tokkyo Koho, 31 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2000159672	A2	20000613	JP 1999-337606	19991129
US 6225315	B1	20010501	US 1999-442821	19991118
EP 1022026	A2	20000726	EP 1999-309406	19991125
EP 1022026	A3	20020410		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2290766	C	20030204	CA 1999-2290766	19991126
ZA 9907371	A	20010529	ZA 1999-7371	19991129
NZ 515501	A	20030829	NZ 1999-515501	19991129
AU 9961788	A1	20000601	AU 1999-61788	19991130
AU 767452	B2	20031113		
KR 2000035774	A	20000626	KR 1999-53785	19991130

PRAI US 1998-110335P P 19981130
OS MARPAT 133:22405
GI



I

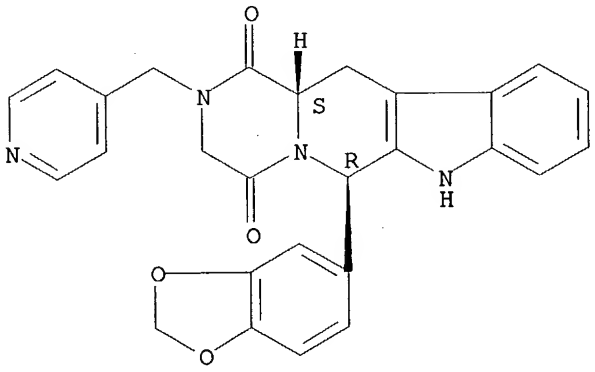
AB The title compds. [I; R1 = H, C1-3 alkyl, C3-5 cycloalkyl, C1-3 perfluoroalkyl; R2 = H, C1-3 perfluoroalkyl, C1-6 alkyl substituted by OH, C1-3 alkoxy, or C3-6 cycloalkyl; R3 = C1-6 alkyl, C3-6 alkenyl, C3-6 alkynyl, C3-7 cycloalkyl, C1-6 perfluoroalkyl, C3-6 cycloalkyl-C1-6 alkyl; R4 together with the R4-bonded N completes 4-N-R6-piperazinyl; R5 = H, C1-4 alkyl, C1-3 alkoxy, NR7R8, CONR7R8; wherein R6 = H, C1-6 alkyl, hydroxy-C2-6 alkyl, R7R8N-C2-6 alkyl, R7R8NCO-C1-6 alkyl, CONR7R8, CSNR7R8, C(:NH)NR7R8; wherein R7, R8 = H, C1-4 alkyl, C1-3 alkoxy-C2-4 alkyl, hydroxy-C2-4 alkyl], pharmacol. acceptable salts, prodrugs, polymorphs, hydrates, solvates, active metabolites, or stereoisomers

thereof , which are cGMP phosphodiesterase inhibitors and useful for the prevention of nitrate tolerance (no data), are prepd. The title compds. also include pyrazolo[3,4-d]pyrimidin-4-one, quinazolin-4-one, purin-6-one, pyrido[3,2-d]pyrimidin-4-one, and pyrazino[1',2':1,6]pyrido[3,4-b]indole derivs.

IT **171488-10-1P 171488-15-6P 171596-29-5P 171596-30-8P 171596-32-0P 171596-36-4P 171596-40-0P 187935-15-5P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preventives contg. 1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one derivs. and related compds. as cGMP phosphodiesterase inhibitors for nitric acid-induced tolerance)

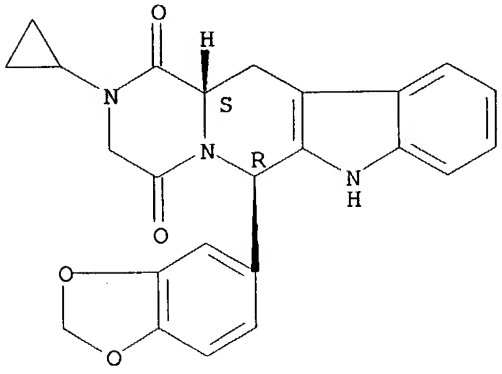
RN 171488-10-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(4-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 171488-15-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopropyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

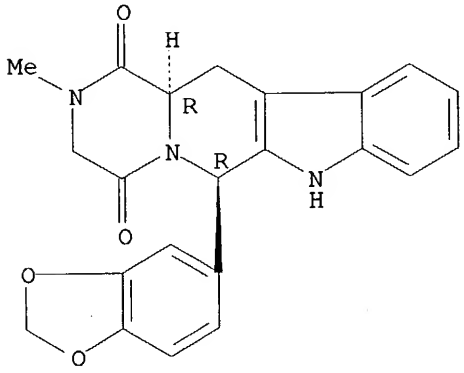
Relative stereochemistry.



RN 171596-29-5 CAPLUS

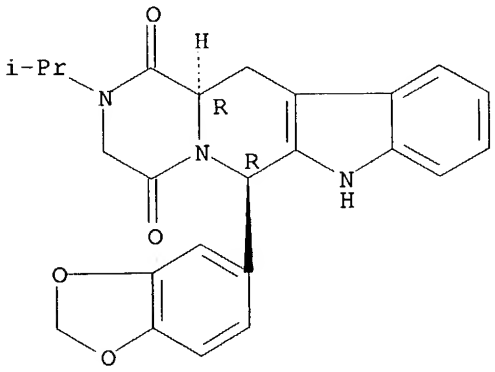
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



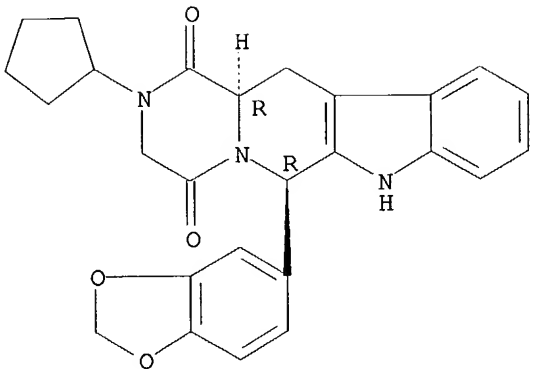
RN 171596-30-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(1-methylethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



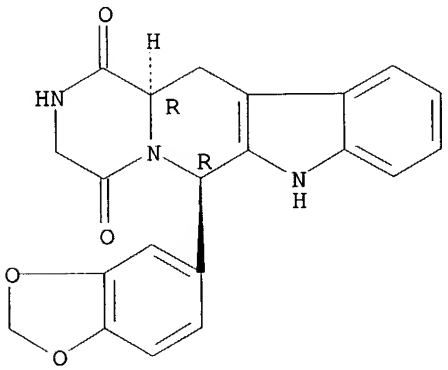
RN 171596-32-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopentyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



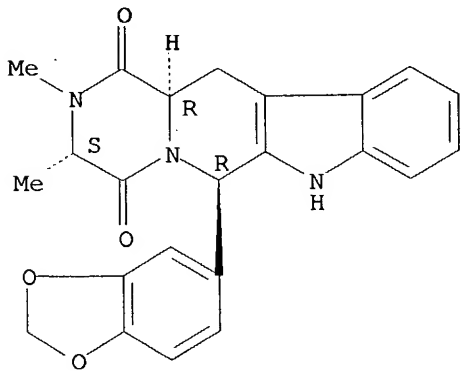
RN 171596-36-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



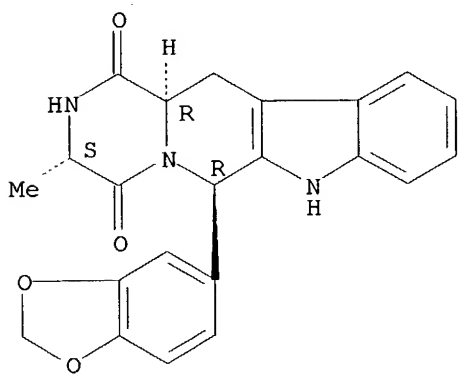
RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 187935-15-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-methyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

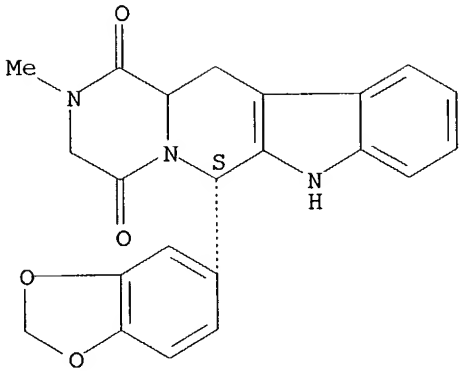


L5 ANSWER 74 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:240994 CAPLUS
DN 132:270098
TI Tablets immediately disintegrating in the oral cavity
IN Furitsu, Hisao; Kato, Akira; Ohwaki, Takayuki; Yasui, Masanori
PA Eisai Co., Ltd., Japan
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000020033	A1	20000413	WO 1999-JP5298	19990928
	W: CA, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2346350	AA	20000413	CA 1999-2346350	19990928
	EP 1120120	A1	20010801	EP 1999-944874	19990928
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000178204	A2	20000627	JP 1999-276133	19990929
	JP 2000191518	A2	20000711	JP 1999-276134	19990929
PRAI	JP 1998-282378	A	19981005		
	JP 1998-295947	A	19981019		
	WO 1999-JP5298	W	19990928		

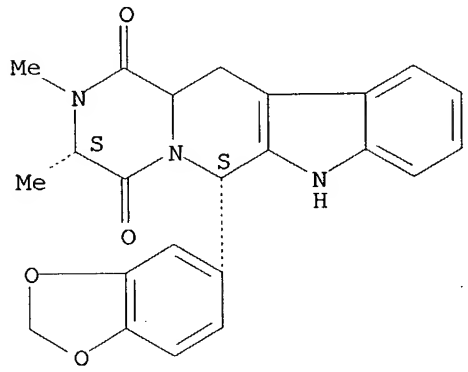
OS MARPAT 132:270098
AB The invention relates to tablets immediately disintegrating in the oral cavity which contain a phosphodiesterase inhibitor having an effect of ameliorating erectile dysfunction and a process for producing the same; and tablets immediately disintegrating in the oral cavity which contain a hardly sol. drug and show an improved soly.; and a process for producing the same. Namely, tablets immediately disintegrating in the oral cavity which contain a cyclic GMP phosphodiesterase inhibitor [e.g. sildenafil] and saccharides and process for producing the same; and a process for producing tablets immediately disintegrating in the oral cavity which comprises dissolving the hardly sol. drug together with a surfactant and/or a water-sol. polymer in an org. solvent or an aq. org. solvent, mixing saccharides with a molded matter obtained by coating a filler or granulating together with a filler, adding an org. solvent, water or an aq. org. solvent thereto, kneading the resultant mixt. and then compression molding the same.
IT **263392-02-5 263392-03-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tablets immediately disintegrating in the oral cavity)
RN 263392-02-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 263392-03-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 75 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:753072 CAPLUS
DN 131:346565
TI Combination of phentolamine and cyclic GMP phosphodiesterase inhibitors for the treatment of sexual dysfunction
IN Estok, Thomas Mark
PA Schering Corporation, USA
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

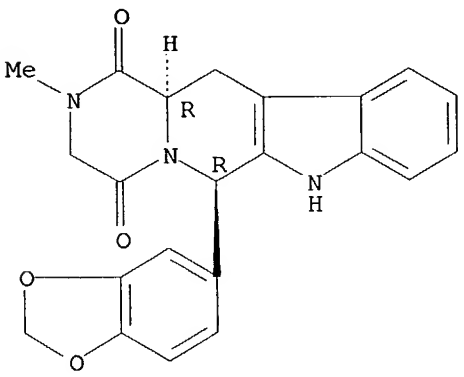
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9959584	A1	19991125	WO 1999-US7046	19990517
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9940685	A1	19991206	AU 1999-40685	19990517
PRAI	US 1998-81640	A	19980520		
	US 1998-82977	A2	19980521		
	US 1998-106517	A	19980629		
	WO 1999-US7046	W	19990517		

AB A method of treating sexual dysfunction comprising administering a therapeutically effective amt. of a combination of phentolamine and cGMP PDE inhibitor (e.g. sildenafil), as well as pharmaceutical compns. and kits useful in those methods, are disclosed.

IT **171596-29-5 171596-40-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phentolamine and cyclic GMP phosphodiesterase inhibitors for the treatment of sexual dysfunction)

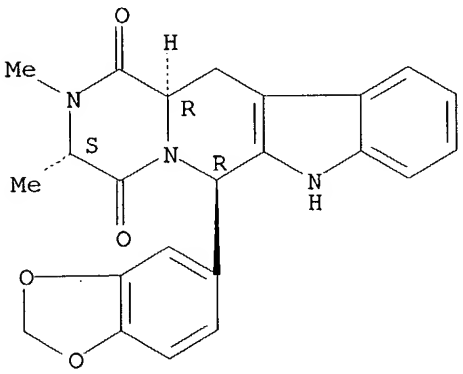
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

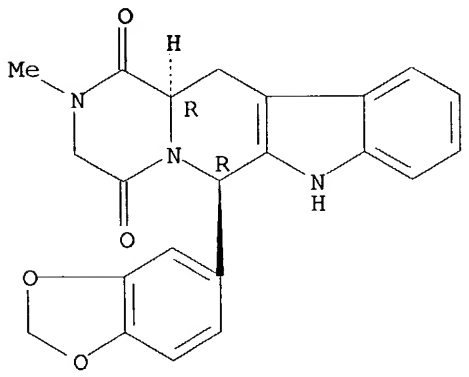
Absolute stereochemistry. Rotation (+).



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 76 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:393867 CAPLUS
DN 131:193591
TI IC-351 ICOS Corp
AU Norman, Peter
CS Norman Consulting, Bucks, SL1 8JW, UK
SO Current Opinion in Central & Peripheral Nervous System Investigational Drugs (1999), 1(2), 268-271
CODEN: COCDFA; ISSN: 1464-844X
PB Current Drugs Ltd.
DT Journal; General Review
LA English
AB A review with 35 refs. IC-351 (GF-196960), an inhibitor of phosphodiesterase 5 (PDE5) from ICOS Corp, is in phase II trials for the treatment of mild to moderate erectile dysfunction (ED) [274568], [296831]. A randomized, placebo-controlled, crossover study assessed the safety and physiol. effects of IC-351 in patients with ED [274568]. Enrollment was completed in Apr. 1998 [284935]. Results from the trial showed that IC-351 demonstrated significant benefit over placebo [311566]. In Oct. 1998, ICOS entered into a joint venture agreement with Eli Lilly for the development and commercialization of IC-351 for the treatment of sexual dysfunction [300118], [310951]. IC-351 is also in development for the treatment of female sexual dysfunction [321995]. In Mar. 1998, the company announced that the compd. was in preclin. evaluation for the treatment of hypertension [284638]. A collaboration with Glaxo Wellcome (GW) was terminated in Mar. 1997 [240438] and intellectual property rights were assigned to ICOS. This left ICOS to develop the compds. with royalties payable to GW. Although GW reserved the right to pursue its own program, it does not appear to be doing so. In Feb. 1999 Deutsche Bank predicted sales of $200 million in 2002 rising to $400 million in 2003 for IC-351 [316821].
IT **171596-29-5**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(effect of IC-351 for treatment of mild to moderate erectile dysfunction)
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 77 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:215760 CAPLUS
DN 126:203727
TI Use of cGMP-phosphodiesterase inhibitors to treat impotence
IN Daugan, Alain Claude-Marie
PA Laboratoire Glaxo Wellcome S.A., Fr.; Daugan, Alain Claude-Marie
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9703675	A1	19970206	WO 1996-EP3024	19960711
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
	CA 2226784	AA	19970206	CA 1996-2226784	19960711
	CA 2226784	C	20030708		
	AU 9664191	A1	19970218	AU 1996-64191	19960711
	AU 704955	B2	19990513		
	EP 839040	A1	19980506	EP 1996-923985	19960711
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
	CN 1195290	A	19981007	CN 1996-196723	19960711
	CN 1112928	B	20030702		
	BR 9609758	A	19990126	BR 1996-9758	19960711
	JP 11509221	T2	19990817	JP 1996-506248	19960711
	IL 122870	A1	20020310	IL 1996-122870	19960711
	CZ 289686	B6	20020313	CZ 1998-33	19960711
	RU 2181288	C2	20020420	RU 1998-102398	19960711
	NO 9800153	A	19980310	NO 1998-153	19980113
	US 6140329	A	20001031	US 1998-981989	19980310
	US 6143746	A	20001107	US 1998-154051	19980916
	US 6608065	B1	20030819	US 2000-573905	20000518
	CZ 289832	B6	20020417	CZ 2000-3428	20000919
PRAI	GB 1995-14464	A	19950714		
	GB 1994-1090	A	19940121		
	WO 1995-EP183	A2	19950119		
	GB 1995-14465	A	19950714		
	CZ 1998-33	A3	19960711		
	WO 1996-EP3024	W	19960711		
	WO 1996-EP3025	A2	19960711		
	US 1998-981989	A1	19980310		

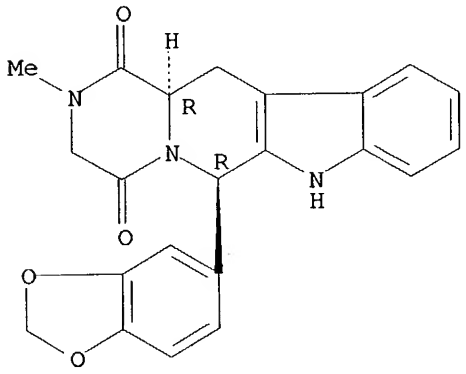
OS MARPAT 126:203727
AB Compds. such as (6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione, (3S,6R,12aR)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione, and physiol. acceptable salts and solvates thereof, can be used as cGMP-phosphodiesterase inhibitors in the treatment of impotence.
IT **171596-29-5P 171596-40-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cGMP-phosphodiesterase inhibitor formulations to treat impotence)

RN 171596-29-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

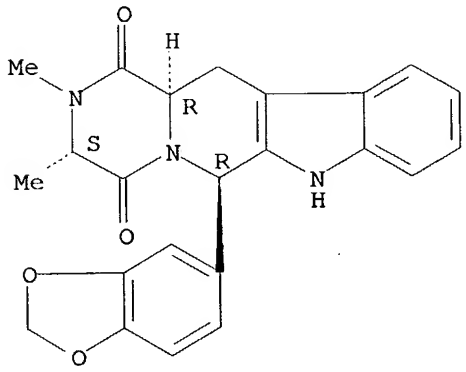
Absolute stereochemistry. Rotation (+).



RN 171596-40-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **187935-15-5P**

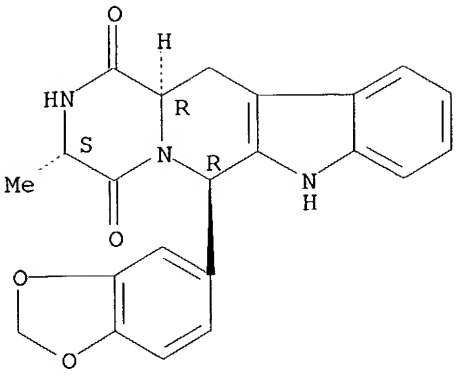
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cGMP-phosphodiesterase inhibitor formulations to treat impotence)

RN 187935-15-5 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-3-methyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.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L5 ANSWER 78 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:101617 CAPLUS
DN 126:108935
TI Method of producing a solid dispersion of a poorly water-soluble drug
IN Butler, James Matthew
PA Glaxo Group Limited, UK; Butler, James Matthew
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

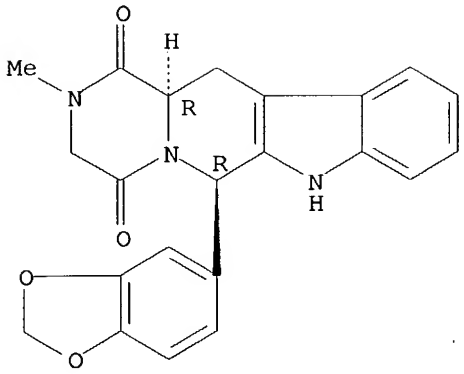
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9638131	A1	19961205	WO 1996-EP2299	19960530
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
	AU 9660026	A1	19961218	AU 1996-60026	19960530
	EP 828479	A1	19980318	EP 1996-917457	19960530
	EP 828479	B1	20011024		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	AT 207344	E	20011115	AT 1996-917457	19960530
	ES 2167566	T3	20020516	ES 1996-917457	19960530
	US 5985326	A	19991116	US 1998-952938	19980206
PRAI	GB 1995-11220	A	19950602		
	WO 1996-EP2299	W	19960530		

AB A process for prepg. solid dispersions of poorly sol. drugs comprises (1) providing an intimate mixt. contg. the carrier or excipient and a nonaq. water-miscible solvent, and optionally, water, (2) mixing the intimate mixt. with the poorly water-sol. drug, and (3) pptg. the drug and the carrier or excipient. Specifically, solid dispersions of (6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione (I) and (+)-N-[1-(adamantanmethyl)-2,4-dioxo-5-phenyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepin-3-yl]-N'-phenylurea are described. I 1 g and hydroxypropyl Me cellulose phthalate 1 g were dissolved in a 9:1 mixt. of acetone/water (27 mL) and 0.25 M HCl 83 mL was added to obtain a ppt. The ppt. was filtered, washed with water, dried, and milled. A tablet contg. 100 mg ppt. was formulated.

IT **171596-29-5P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrazinopyridoindole deriv. in manuf. of solid dispersion of poorly water-sol. drugs)

RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).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L5 ANSWER 79 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1995:986316 CAPLUS
DN 124:55977
TI Preparation of pyrazinopyridoindolediones as inhibitors of cyclic guanosine 3',5'-monophosphate specific phosphodiesterase
IN Daugan, Alain Claude-Marie
PA Laboratoires Glaxo S.A., Fr.
SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9519978	A1	19950727	WO 1995-EP183	19950119
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
HR 950023	B1	20001031	HR 1995-950023	19950117
TW 378210	B	20000101	TW 1995-84100415	19950118
CA 2181377	AA	19950727	CA 1995-2181377	19950119
CA 2181377	C	20020528		
AU 9515748	A1	19950808	AU 1995-15748	19950119
AU 689205	B2	19980326		
ZA 9500424	A	19950927	ZA 1995-424	19950119
EP 740668	A1	19961106	EP 1995-907565	19950119
EP 740668	B1	19980729		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1143963	A	19970226	CN 1995-192078	19950119
CN 1045777	B	19991020		
HU 74943	A2	19970328	HU 1996-1982	19950119
JP 09508113	T2	19970819	JP 1995-519339	19950119
BR 9506559	A	19971028	BR 1995-6559	19950119
AT 169018	E	19980815	AT 1995-907565	19950119
IL 112384	A1	19980816	IL 1995-112384	19950119
ES 2122543	T3	19981216	ES 1995-907565	19950119
RU 2142463	C1	19991210	RU 1996-117127	19950119
CZ 286566	B6	20000517	CZ 1996-2116	19950119
SK 280879	B6	20000814	SK 1996-940	19950119
PL 179744	B1	20001031	PL 1995-315559	19950119
RO 117794	B1	20020730	RO 1996-1454	19950119
IN 183942	A	20000520	IN 1995-DE77	19950120
LV 11690	B	19970620	LV 1996-228	19960710
US 5859006	A	19990112	US 1996-669389	19960716
FI 9602927	A	19960719	FI 1996-2927	19960719
NO 9603015	A	19960909	NO 1996-3015	19960719
AU 9873912	A1	19980820	AU 1998-73912	19980626
AU 707055	B2	19990701		
US 6025494	A	20000215	US 1998-133078	19980812
US 6143746	A	20001107	US 1998-154051	19980916
CN 1224720	A	19990804	CN 1998-122779	19981201
CN 1070492	B	20010905		
HK 1013286	A1	20000519	HK 1998-114572	19981222
US 6127542	A	20001003	US 1999-399667	19990921

	US 6369059	B1	20020409	US 2000-633431	20000807
	US 2002119976	A1	20020829	US 2002-68114	20020205
PRAI	GB 1994-1090	A	19940121		
	WO 1995-EP183	W	19950119		
	GB 1995-14464	A	19950714		
	GB 1995-14465	A	19950714		
	WO 1996-EP3024	A2	19960711		
	WO 1996-EP3025	A2	19960711		
	US 1996-669389	A3	19960716		
	US 1998-133078	A1	19980812		
	US 1999-399667	A1	19990921		
	US 2000-633431	A1	20000807		

OS MARPAT 124:55977

GI For diagram(s), see printed CA Issue.

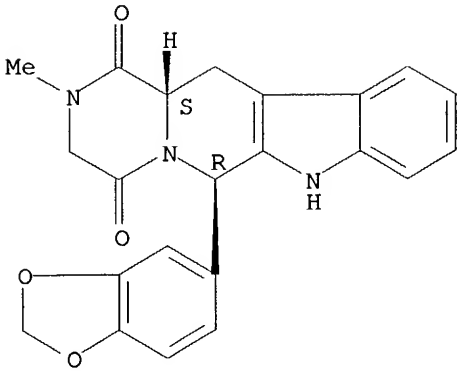
AB The title compds. I [R represents hydrogen, halogen or C1-6 alkyl; R1 represents hydrogen, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, haloC1-6alkyl, C3-8cycloalkyl, etc.; R2 represents an optionally substituted monocyclic arom. ring selected from benzene, thiophene, furan and pyridine or an optionally substituted bicyclic ring Q1 attached to the rest of the mol. via one of the benzene ring carbon atoms and wherein the fused ring A is a 5- or 6-membered ring which may be satd. or partially or fully unsatd. and comprises carbon atoms and optionally one or two heteroatoms selected from oxygen, sulfur and nitrogen; and R3 represents hydrogen or C1-3 alkyl, or R1 and R3 together represent a 3- or 4-membered alkyl or alkenyl chain] are prepd. In an in vitro test for inhibitory effect on cGMP-PDE, cis-2,3,6,7,12,12a-hexahydro-2-(4-pyridylmethyl)-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione (prepn. given) showed IC50 of 10 nM.

IT **171488-01-0P 171488-03-2P 171488-04-3P**
171488-06-5P 171488-07-6P 171488-08-7P
171488-09-8P 171488-10-1P 171488-11-2P
171488-12-3P 171488-13-4P 171488-14-5P
171488-15-6P 171488-16-7P 171488-17-8P
171488-18-9P 171488-19-0P 171488-20-3P
171488-21-4P 171488-22-5P 171488-76-9P
171488-77-0P 171488-86-1P 171488-87-2P
171488-91-8P 171488-92-9P 171488-93-0P
171488-94-1P 171488-95-2P 171489-02-4P
171596-27-3P 171596-28-4P 171596-29-5P
171596-30-8P 171596-31-9P 171596-32-0P
171596-36-4P 171596-40-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrazinopyridoindolediones as inhibitors of cyclic guanosine monophosphate specific phosphodiesterase)

RN 171488-01-0 CAPLUS

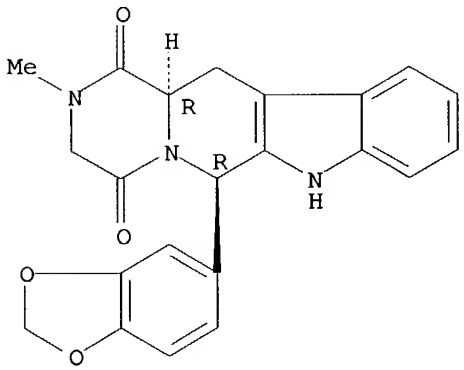
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



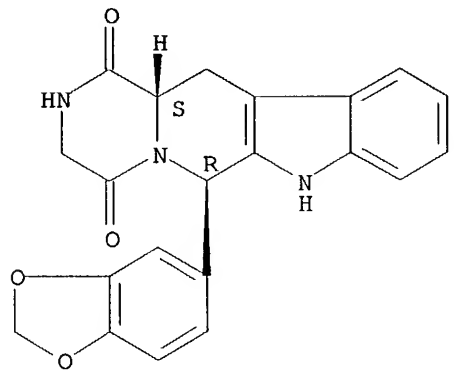
RN 171488-03-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



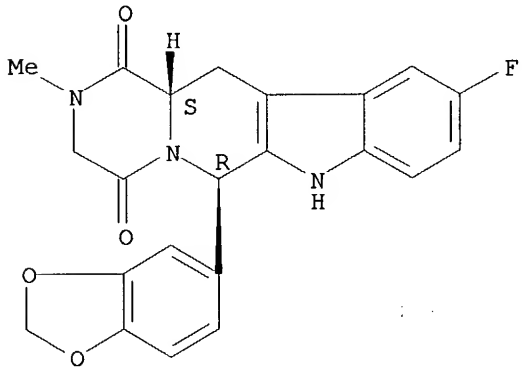
RN 171488-04-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



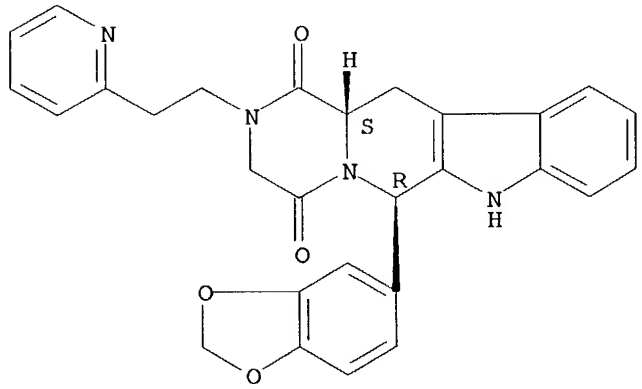
RN 171488-06-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-10-fluoro-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



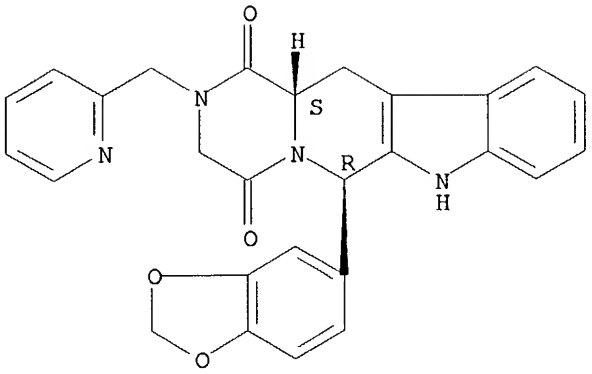
RN 171488-07-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-[2-(2-pyridinyl)ethyl]-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



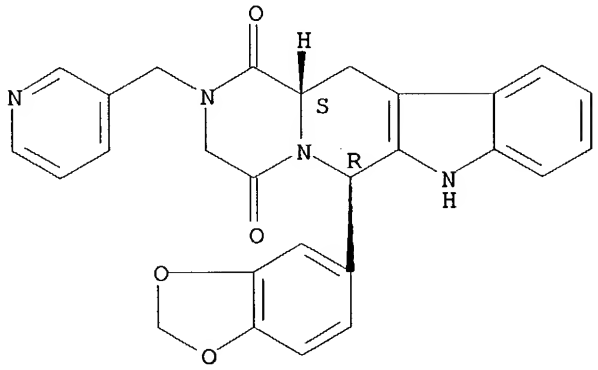
RN 171488-08-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



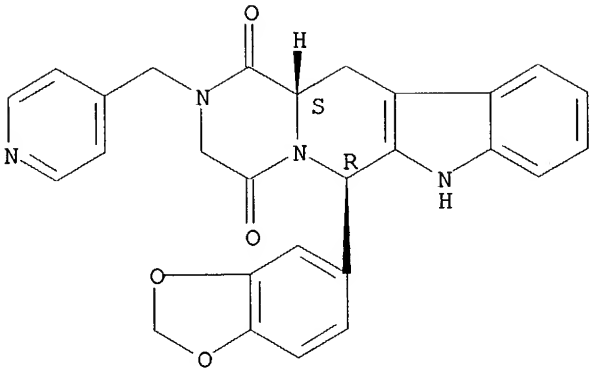
RN 171488-09-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(3-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



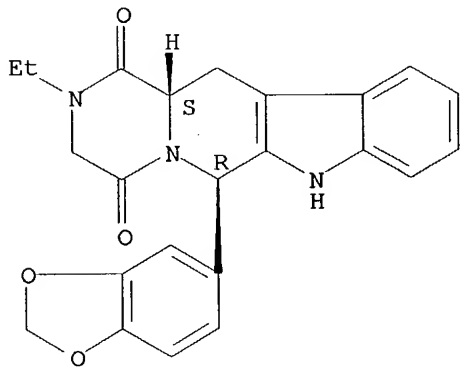
RN 171488-10-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(4-pyridinylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



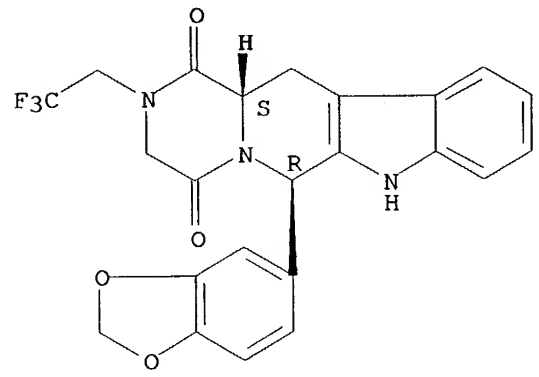
RN 171488-11-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-ethyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



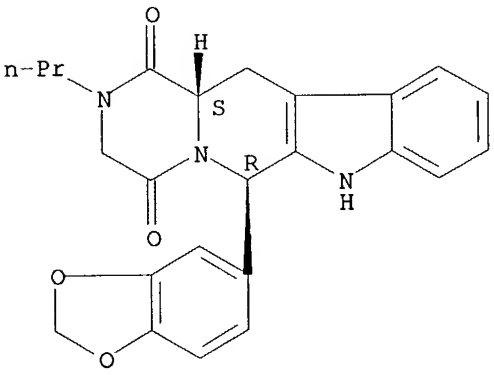
RN 171488-12-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2,2,2-trifluoroethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



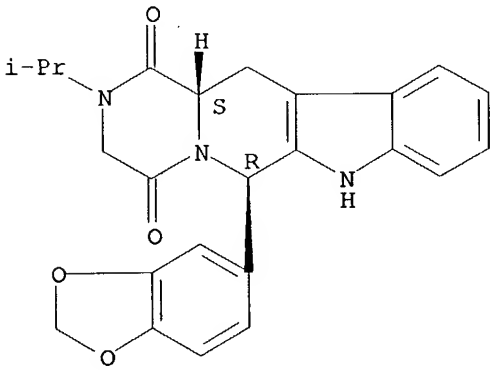
RN 171488-13-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-propyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



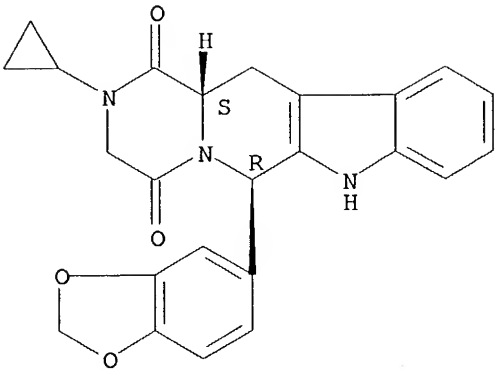
RN 171488-14-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(1-methylethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



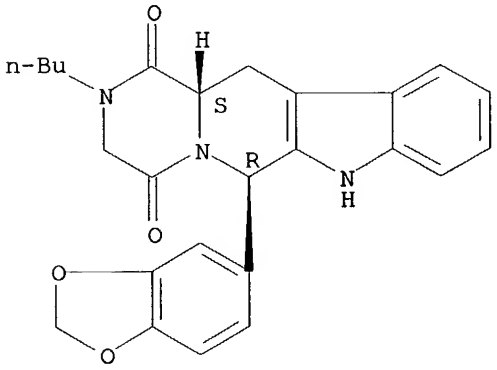
RN 171488-15-6 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopropyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



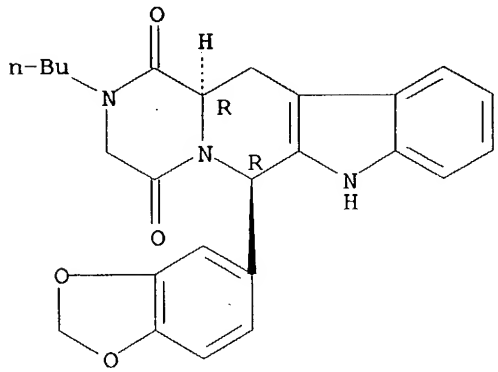
RN 171488-16-7 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



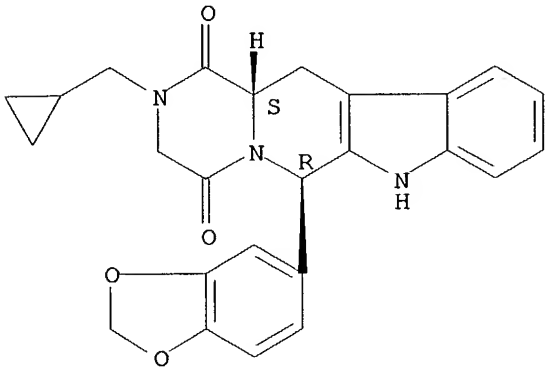
RN 171488-17-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



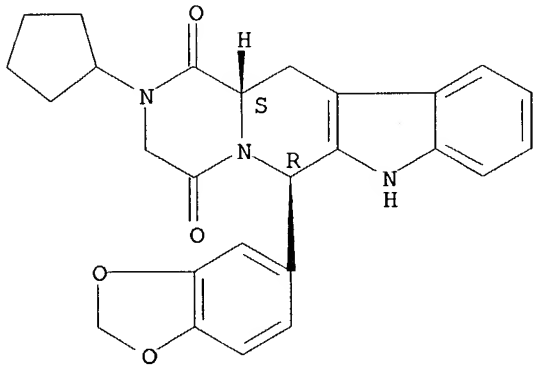
RN 171488-18-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(cyclopropylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



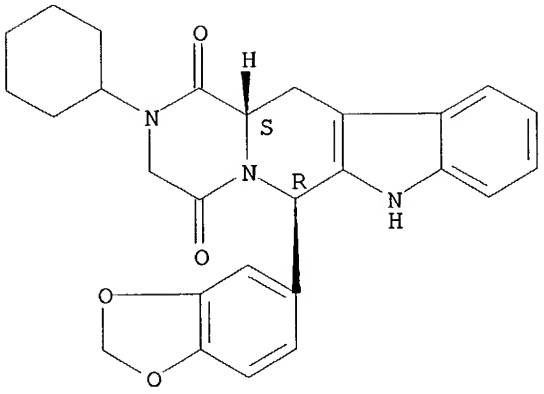
RN 171488-19-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopentyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



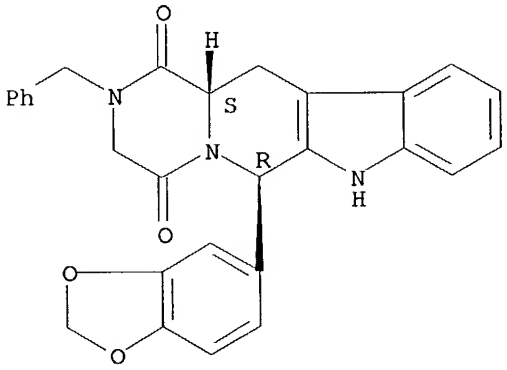
RN 171488-20-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclohexyl-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



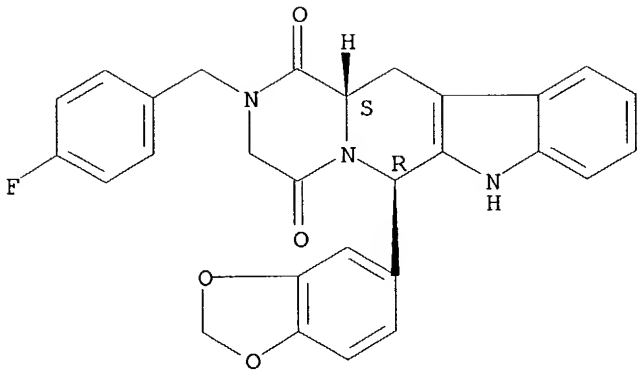
RN 171488-21-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(phenylmethyl)-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



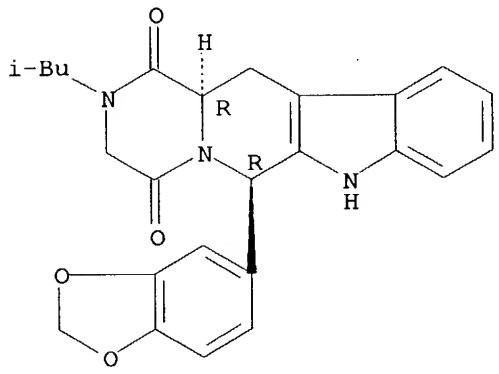
RN 171488-22-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[(4-fluorophenyl)methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



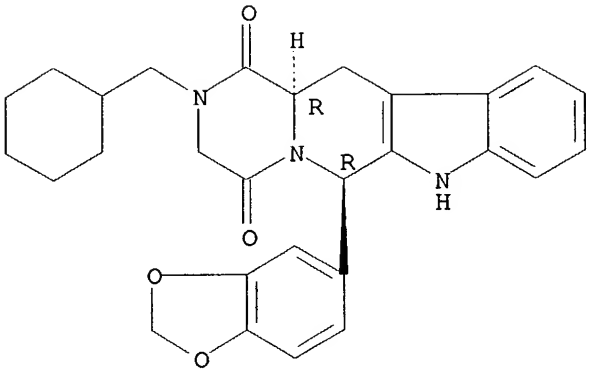
RN 171488-76-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-methylpropyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



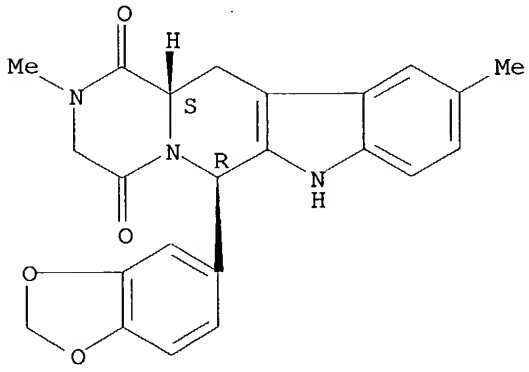
RN 171488-77-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(cyclohexylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



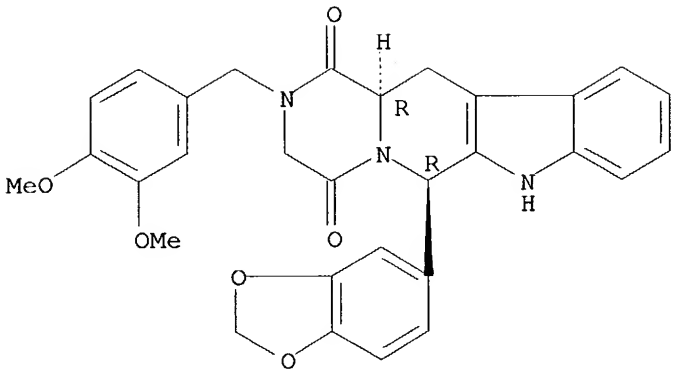
RN 171488-86-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,10-dimethyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



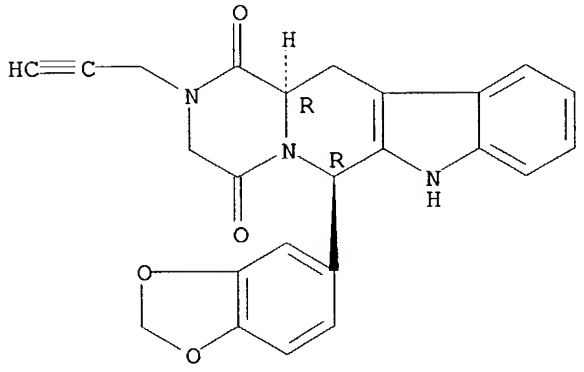
RN 171488-87-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[(3,4-dimethoxyphenyl)methyl]-2,3,6,7,12,12a-hexahydro-, (6R,12aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



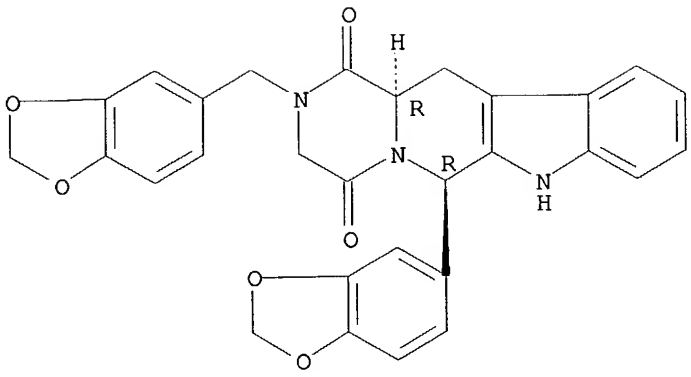
RN 171488-91-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-propynyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



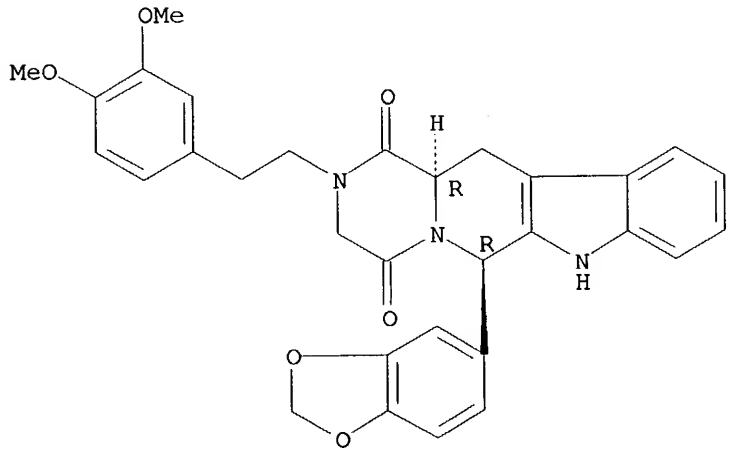
RN 171488-92-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(1,3-benzodioxol-5-ylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



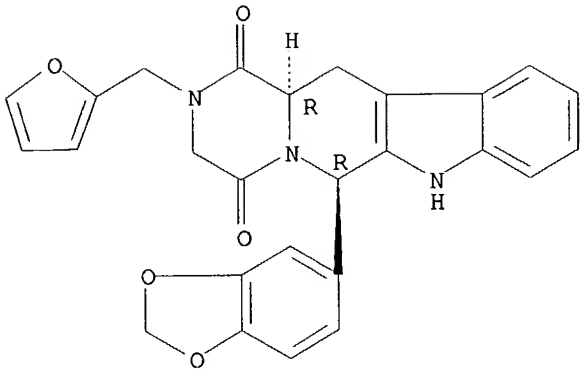
RN 171488-93-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-[2-(3,4-dimethoxyphenyl)ethyl]-2,3,6,7,12,12a-hexahydro-, (6R-trans)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



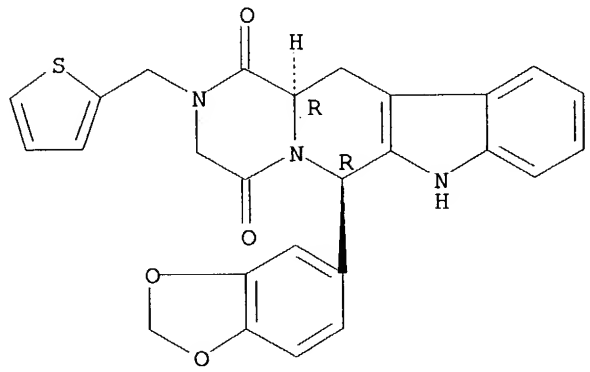
RN 171488-94-1 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-(2-furanylmethyl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



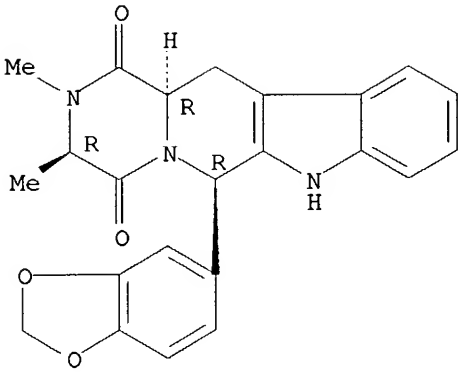
RN 171488-95-2 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(2-thienylmethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



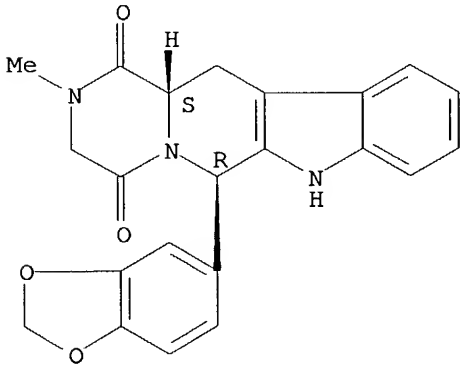
RN 171489-02-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3R,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



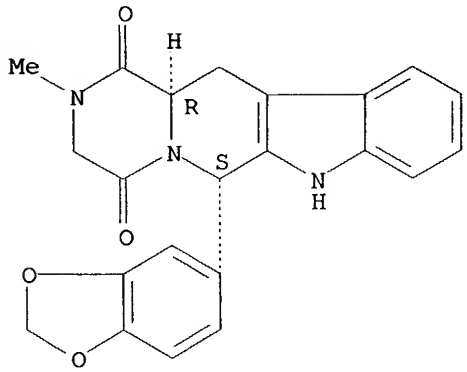
RN 171596-27-3 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



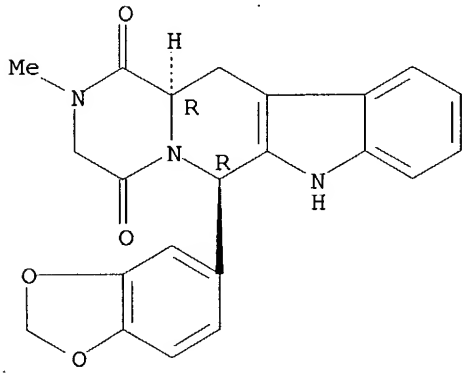
RN 171596-28-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6S,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



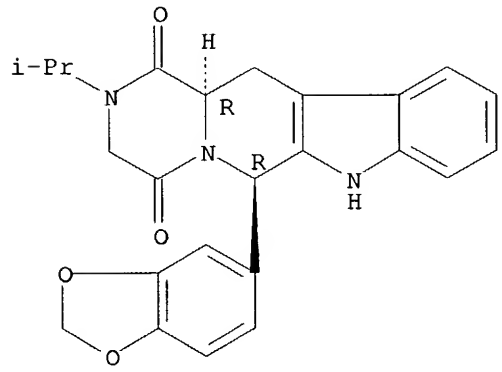
RN 171596-29-5 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



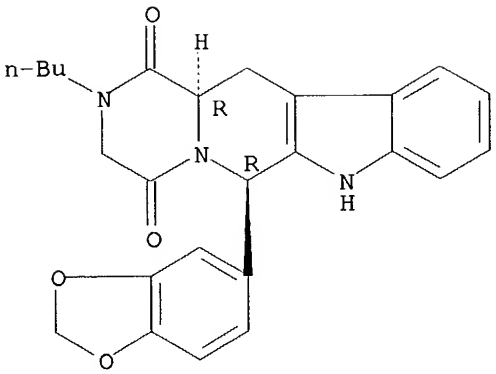
RN 171596-30-8 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-(1-methylethyl)-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



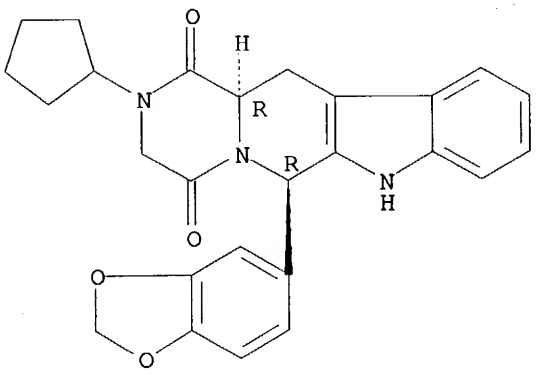
RN 171596-31-9 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-butyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



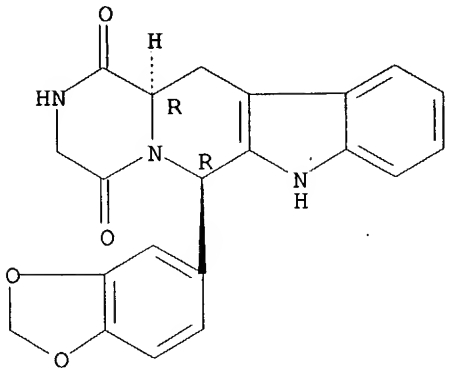
RN 171596-32-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2-cyclopentyl-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



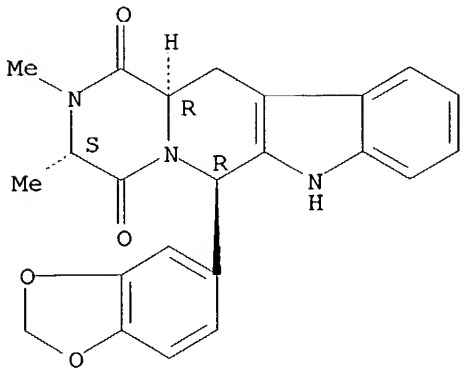
RN 171596-36-4 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-, (6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 171596-40-0 CAPLUS
CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-, (3S,6R,12aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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L5 ANSWER 68 OF 79 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:785898 CAPLUS
DN 133:329627
TI Tetracyclic cGMP-specific phosphodiesterase inhibitors and their use in disease treatment
IN Daugan, Alain Claude Marie; Gellibert, Francoise
PA Icos Corp., USA
SO U.S., 30 pp., Cont.-in-part of PCT 9519978.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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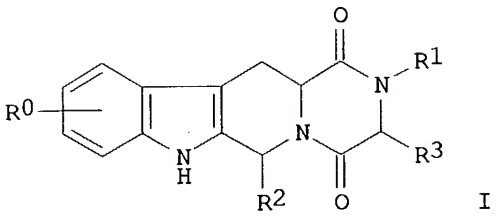

I

AB A compd. of formula I (R0 = H, halogen, C1-6 alkyl; R1 = H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, halo-C1-6 alkyl, C3-8 cycloalkyl, C3-8 cycloalkyl-C1-3 alkyl, aryl-C1-3 alkyl, heteroaryl-C1-3 alkyl; R2 = (substituted) monocyclic arom. ring selected from benzene, thiophene, furan, and pyridine, or (substituted) bicyclic ring (a) attached to the rest of the mol. via one of the benzene ring carbon atoms, and wherein the fused ring is a 5- or 6-membered ring which may be satd. or partially or fully unsatd., and comprises carbon atoms and optionally one or two heteroatoms selected from oxygen, sulfur, and nitrogen; R3 = H, C1-3 alkyl, or R1 and R3 together = 3- or 4-membered alkyl or alkenyl chain) and salts and solvates thereof is disclosed. Compd. I is a potent and selective inhibitor of cyclic guanosine 3',5'-monophosphate-specific phosphodiesterase, having a utility in a variety of therapeutic areas where such inhibition is beneficial, including the treatment of cardiovascular disorders and erectile dysfunction. Thus, many I compds. were synthesized and tested in vitro as inhibitors of cGMP phosphodiesterase. Cis-2,3,6,7,12,12a-hexahydro-2-(4-pyridylmethyl)-6-(3,4-methylenedioxyphenyl)pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione showed IC50 of 10 nM.

IT **171488-01-0P 171488-03-2P 171488-04-3P**
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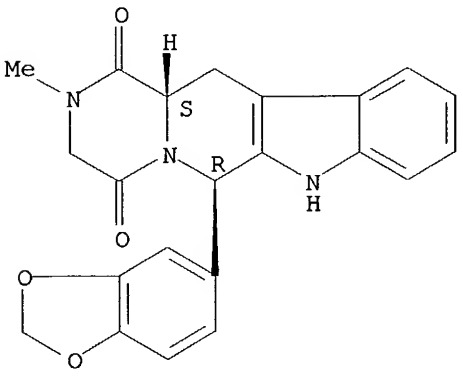
171596-40-0P 187935-15-5P 303984-32-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tetracyclic cyclic GMP-specific phosphodiesterase inhibitors and their use in disease treatment)

RN 171488-01-0 CAPLUS

CN Pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione, 6-(1,3-benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-methyl-, (6R,12aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



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Relative stereochemistry.